```
=> d his nofile

     (FILE 'HOME' ENTERED AT 10:22:35 ON 16 JUN 2006)

     FILE 'CAPLUS' ENTERED AT 10:22:50 ON 16 JUN 2006
                E US2003-603406/APPS
L1            1 SEA ABB=ON  PLU=ON  US2003-603406/AP
                D SCAN
                SEL RN L1

     FILE 'REGISTRY' ENTERED AT 10:23:15 ON 16 JUN 2006
L2           28 SEA ABB=ON  PLU=ON  (7689-03-4/BI OR 100286-90-6/BI OR
                104615-18-1/BI OR 114977-28-5/BI OR 139180-30-6/BI OR 1404-19-9
                /BI OR 142243-02-5/BI OR 142805-58-1/BI OR 14343-69-2/BI OR
                150316-14-6/BI OR 154-17-6/BI OR 165245-96-5/BI OR 2001-95-8/BI
                 OR 23214-92-8/BI OR 252979-43-4/BI OR 33069-62-4/BI OR
                361484-63-1/BI OR 361484-64-2/BI OR 396653-58-0/BI OR 53643-48-
                4/BI OR 56-65-5/BI OR 581-64-6/BI OR 5854-93-3/BI OR 638195-73-
                0/BI OR 638195-74-1/BI OR 638195-75-2/BI OR 865-21-4/BI OR
                9027-72-9/BI)
                D SCAN
L3              STRUCTURE UPLOADED
L4           12 SEA SSS SAM L3
L5          186 SEA SSS FUL L3

     FILE 'CAPLUS' ENTERED AT 10:27:27 ON 16 JUN 2006
L6           34 SEA ABB=ON  PLU=ON  L5
L7           15 SEA ABB=ON  PLU=ON  L6 NOT (PY>2002 OR AY>2002 OR PRY>2002)
                E BOREA P/AU
L8          284 SEA ABB=ON  PLU=ON  ("BOREA P"/AU OR "BOREA P A"/AU OR "BOREA
                PIER A"/AU OR "BOREA PIER ANDREA"/AU OR "BOREA PIERANDREA"/AU
                OR "BOREA PIERO A"/AU OR "BOREA PIERO ANDREA"/AU)
                E BARALDI P/AU
L9          307 SEA ABB=ON  PLU=ON  ("BARALDI P"/AU OR "BARALDI P G"/AU OR
                "BARALDI PIER G"/AU OR "BARALDI PIER GIOVANI"/AU OR "BARALDI
                PIER GIOVANNI"/AU OR "BARALDI PIERGIOVANNI"/AU OR "BARALDI
                PIERO"/AU)
L10       22385 SEA ABB=ON  PLU=ON  CHEN S?/AU
                E LEUNG E/AU
L11         108 SEA ABB=ON  PLU=ON  ("LEUNG E"/AU OR "LEUNG E M"/AU OR "LEUNG
                E M W"/AU OR "LEUNG E S"/AU OR "LEUNG E T Y"/AU OR "LEUNG E
                Y"/AU OR "LEUNG E Y W"/AU OR "LEUNG EDWARD"/AU OR "LEUNG
                EDWARD C W"/AU OR "LEUNG EDWARD K Y"/AU OR "LEUNG EDWARD M
                F"/AU)
L12          72 SEA ABB=ON  PLU=ON  (L8 AND (L9 OR L10 OR L11)) OR (L9 AND
                (L10 OR L11)) OR (L10 AND L11)
                E MDR/CT
                E E3+ALL
                E ADENOSINE/CT
                E E3+ALL
L13       92844 SEA ABB=ON  PLU=ON  ((MDR (2A)CANCER?) OR ADENOSINE?)/BI,OBI
L14          65 SEA ABB=ON  PLU=ON  L13 AND L12
L15          60 SEA ABB=ON  PLU=ON  L14 AND (A3 OR ANTAGONIST?)/OBI,BI
L16          24 SEA ABB=ON  PLU=ON  L14 AND (ADENOSINE(2A)A3(2A)ANTAGONIST?)/OB
                I,BI
L17          24 SEA ABB=ON  PLU=ON  L12 AND (ADENOSINE(2A)A3(2A)ANTAGONIST?)/OB
                I,BI
L18           2 SEA ABB=ON  PLU=ON  L17 AND MDR?/OBI
L19           2 SEA ABB=ON  PLU=ON  L12 AND (MDR?)/OBI,BI
```

```
L20          20 SEA ABB=ON  PLU=ON  L12 AND (CANCER? OR TUMOR? OR TUMOUR? OR
                NEOPLASM? OR GROWTH?)/OBI,BI
L21          40 SEA ABB=ON  PLU=ON  (L16 OR L17 OR L18 OR L19 OR L20)
L22          19 SEA ABB=ON  PLU=ON  L20 AND (ADENOSINE?)/OBI,BI
L23          40 SEA ABB=ON  PLU=ON  (L21 OR L22)
                D BIB
L24          71 SEA ABB=ON  PLU=ON  (L8 AND (L9 OR L10 OR L11))
L25          21 SEA ABB=ON  PLU=ON  (L9 AND (L10 OR L11))
L26           2 SEA ABB=ON  PLU=ON  (L10 AND L11)
L27          20 SEA ABB=ON  PLU=ON  (L24 AND (L25 OR L26)) OR (L25 AND L26)
L28          47 SEA ABB=ON  PLU=ON  (L23 OR L27)
L29          20 SEA ABB=ON  PLU=ON  L27 AND (ADENOSINE? OR MDR? OR CANCER?)/OBI
                ,BI
L30          20 SEA ABB=ON  PLU=ON  L27 AND (ADENOSINE? OR MDR?)/OBI,BI
L31          20 SEA ABB=ON  PLU=ON  L27 AND (ADENOSINE?)/OBI,BI
L32          47 SEA ABB=ON  PLU=ON  (L28 OR L29 OR L30 OR L31)

=> file caplus
FILE 'CAPLUS' ENTERED AT 10:44:06 ON 16 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 16 Jun 2006  VOL 144 ISS 26
FILE LAST UPDATED: 15 Jun 2006  (20060615/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que l32
L8          284 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("BOREA P"/AU OR "BOREA P
                A"/AU OR "BOREA PIER A"/AU OR "BOREA PIER ANDREA"/AU OR "BOREA
                PIERANDREA"/AU OR "BOREA PIERO A"/AU OR "BOREA PIERO ANDREA"/AU
                )
L9          307 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("BARALDI P"/AU OR "BARALDI P
                G"/AU OR "BARALDI PIER G"/AU OR "BARALDI PIER GIOVANI"/AU OR
                "BARALDI PIER GIOVANNI"/AU OR "BARALDI PIERGIOVANNI"/AU OR
                "BARALDI PIERO"/AU)
L10       22385 SEA FILE=CAPLUS ABB=ON  PLU=ON  CHEN S?/AU
L11         108 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("LEUNG E"/AU OR "LEUNG E
                M"/AU OR "LEUNG E M W"/AU OR "LEUNG E S"/AU OR "LEUNG E T
                Y"/AU OR "LEUNG E Y"/AU OR "LEUNG E Y W"/AU OR "LEUNG EDWARD"/A
                U OR "LEUNG EDWARD C W"/AU OR "LEUNG EDWARD K Y"/AU OR "LEUNG
                EDWARD M F"/AU)
L12          72 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L8 AND (L9 OR L10 OR L11)) OR
```

```
                (L9 AND (L10 OR L11)) OR (L10 AND L11)
L13         92844 SEA FILE=CAPLUS ABB=ON  PLU=ON  ((MDR (2A)CANCER?) OR ADENOSINE
                  ?)/BI,OBI
L14            65 SEA FILE=CAPLUS ABB=ON  PLU=ON  L13 AND L12
L16            24 SEA FILE=CAPLUS ABB=ON  PLU=ON  L14 AND (ADENOSINE(2A)A3(2A)ANT
                  AGONIST?)/OBI,BI
L17            24 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 AND (ADENOSINE(2A)A3(2A)ANT
                  AGONIST?)/OBI,BI
L18             2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L17 AND MDR?/OBI
L19             2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 AND (MDR?)/OBI,BI
L20            20 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 AND (CANCER? OR TUMOR? OR
                  TUMOUR? OR NEOPLASM? OR GROWTH?)/OBI,BI
L21            40 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L16 OR L17 OR L18 OR L19 OR
                  L20)
L22            19 SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 AND (ADENOSINE?)/OBI,BI
L23            40 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L21 OR L22)
L24            71 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L8 AND (L9 OR L10 OR L11))
L25            21 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L9 AND (L10 OR L11))
L26             2 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L10 AND L11)
L27            20 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L24 AND (L25 OR L26)) OR (L25
                  AND L26)
L28            47 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L23 OR L27)
L29            20 SEA FILE=CAPLUS ABB=ON  PLU=ON  L27 AND (ADENOSINE? OR MDR? OR
                  CANCER?)/OBI,BI
L30            20 SEA FILE=CAPLUS ABB=ON  PLU=ON  L27 AND (ADENOSINE? OR
                  MDR?)/OBI,BI
L31            20 SEA FILE=CAPLUS ABB=ON  PLU=ON  L27 AND (ADENOSINE?)/OBI,BI
L32            47 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L28 OR L29 OR L30 OR L31)


=> d ibib abs l32 tot

L32  ANSWER 1 OF 47  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2006:539355  CAPLUS
TITLE:                   Adenosine modulates vascular endothelial
                         growth factor expression via hypoxia-inducible
                         factor-1 in human glioblastoma cells
AUTHOR(S):               Merighi, Stefania; Benini, Annalisa; Mirandola,
                         Prisco; Gessi, Stefania; Varani, Katia; Leung,
                         Edward; Maclennan, Stephen; Borea, Pier
                         Andrea
CORPORATE SOURCE:        Department of Clinical and Experimental Medicine,
                         Pharmacology Unit, University of Ferrara, Ferrara,
                         44100, Italy
SOURCE:                  Biochemical Pharmacology (2006), 72(1), 19-31
                         CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER:               Elsevier B.V.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Hypoxia appears to induce a program which shifts the cellular phenotype
     toward an increase in extracellular adenosine.
     Hypoxia-inducible factor-1 (HIF-1) is a key regulator of genes crucial to
     many aspects of cancer biol. Since in gliomas there is a strong
     correlation between HIF-1α expression, tumor grade and
     tumor vascularization, the aim of this study was to investigate
     whether adenosine may regulate HIF-1 in human glioblastoma cell
     lines. The results indicate that in the human hypoxic A172 and U87MG
     glioblastoma cell lines adenosine up-regulates HIF-1α
     protein expression via the A3 receptor subtype. In particular, we
```

investigated the effect of A3 receptor antagonists on HIF-1 and vascular endothelial **growth** factor (VEGF) expression. We found that **A3 antagonists** inhibit **adenosine**-induced HIF-1α and VEGF protein accumulation in the hypoxic cells. Investigations in the mol. mechanism showed that A3 receptor stimulation activates p44/p42 and p38 MAPKs that are required for A3-induced increase of HIF-1α and VEGF. Further studies are required to demonstrate the in vivo relevance of these observations with regard to the proposed role for **adenosine** as a key element in hypoxia and in **tumors**
.

L32 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:496108 CAPLUS
TITLE: Enhancing treatment of HIF-1-mediated disorders with **adenosine** A3 receptor agonists
INVENTOR(S): **Borea, Pier Andrea**; **Baraldi, Pier Giovanni**; Merighi, Stefania; Maclennan, Stephen; **Leung, Edward**; Moorman, Allan
PATENT ASSIGNEE(S): King Pharmaceuticals Research & Development Inc., USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006055970	A2	20060526	WO 2005-US42552	20051122

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-630555P P 20041122
AB The invention discloses the use of **adenosine** receptor agonists, preferably A3 receptor agonists, either alone or in combination with other agents for the treatment, prevention and/or management of diseases or disorders associated with underexpression of HIF-1α and/or decreased HIF-1α activity (e.g., ischemic related disorders). The methods of the invention are directed to methods of reducing tissue damage (e.g., substantially preventing tissue damage, inducing tissue protection) resulting from ischemia or hypoxia. The invention provides methods for treating, preventing and/or ameliorating one or more symptoms of hypoxic or HIF-1α-related disorders by administering an A3 receptor agonist either alone or in combination with other agents.

L32 ANSWER 3 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:106016 CAPLUS
DOCUMENT NUMBER: 144:350631
TITLE: Synthesis and Biological Studies of a New Series of 5-Heteroarylcarbamoylaminopyrazolo[4,3-e]1,2,4-

triazolo[1,5-c]pyrimidines as Human **A3 Adenosine** Receptor **Antagonists**. Influence of the Heteroaryl Substituent on Binding Affinity and Molecular Modeling Investigations

AUTHOR(S): Pastorin, Giorgia; Da Ros, Tatiana; Bolcato, Chiara; Montopoli, Christian; Moro, Stefano; Cacciari, Barbara; **Baraldi, Pier Giovanni**; Varani, Katia; **Borea, Pier Andrea**; Spalluto, Giampiero

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Trieste, Trieste, I-34127, Italy

SOURCE: Journal of Medicinal Chemistry (2006), 49(5), 1720-1729
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Some pyrazolotriazolopyrimidines bearing different heteroarylcarbamoylamino moieties at the N(5)-position are described. The synthesis of a water soluble compound with high potency and selectivity vs. the human **A3 adenosine** receptor as **antagonist** has been reported, and an enlarged series of compds. related to this compound is presented. These compds. showed A3 **adenosine** receptor affinity in the nanomolar range and different levels of selectivity evaluated in radioligand binding assays at human A1, A2A, A2B, and A3 **adenosine** receptors. In particular, the effect of the heteroaryl substituents at the N(5) position has been analyzed. This study leads to the recognition that the presence of a pyridinium moiety in this position not only increases water solubility but also improves or retains potency and selectivity at the human A3 **adenosine** receptors. In contrast, replacement of pyridine with different heterocycles produces loss of affinity and selectivity at the human A3 **adenosine** receptors. A mol. modeling study has been carried out with the aim to explain these various binding profiles.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:87936 CAPLUS

DOCUMENT NUMBER: 144:331196

TITLE: Synthesis and biological characterization of [3H](2-amino-4,5,6,7-tetrahydrobenzo[b]thiophen-3-yl)(4-chlorophenyl)methanone, the first radiolabeled **adenosine** A1 allosteric enhancer

AUTHOR(S): **Baraldi, Pier Giovanni**; Pavani, Maria Giovanna; **Leung, Edward**; Moorman, Allan R.; Varani, Katia; Vincenzi, Fabrizio; **Borea, Pier Andrea**; Romagnoli, Romeo

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy

SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(5), 1402-1404
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Among the **adenosine** A1 allosteric enhancers reported so far, compound (2-amino-4,5,6,7-tetrahydrobenzo[b]thiophen-3-yl)(4-chlorophenyl)methanone (I, named T-62) has shown biol. properties similar

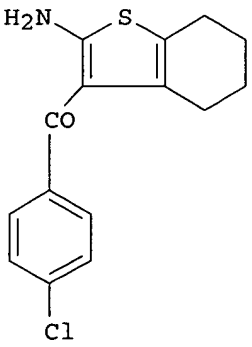
to those of PD 81,723, the reference A1 allosteric enhancer and it has been more fully pharmacol. investigated. The preparation of the radiolabeled form of compound I and its characterization by saturation binding expts. are reported.

These studies allowed us to demonstrate for the first time the existence of a specific, allosteric site on the A1 receptor.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:30092 CAPLUS
DOCUMENT NUMBER: 144:246527
TITLE: Synthesis and biological evaluation of allosteric A1-**adenosine** receptor modulators structurally related to (2-amino-4,5,6,7-tetrahydro-benzo[b]thiophen-3-yl)-(4-chloro-phenyl)- methanone, a potent compound useful to reduce neuropathic pain
AUTHOR(S): Romagnoli, Romeo; **Baraldi, Pier Giovanni**; Pavani, Maria Giovanna; Tabrizi, Mojgan Aghazadeh; Iaconinoto, Maria Antonietta; Carrion, Maria Dora; Cara, Carlota Lopez; Shryock, John C.; **Leung, Edward**; Moorman, Allan R.; Gessi, Stefania; Merighi, Stefania; **Borea, Pier Andrea**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy
SOURCE: Medicinal Chemistry Research (2005), 14(3), 125-142
CODEN: MCREEB; ISSN: 1054-2523
PUBLISHER: Birkhaeuser Boston
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB New derivs. of (2-amino-4,5,6,7-tetrahydrobenzo[b]thiophen-3-yl)-(4-chlorophenyl)methanone (I), an allosteric enhancer of agonist binding to the A1-**adenosine** receptor, have been synthesized and evaluated in an intact cell assay at different concns. to determine which among them were potential allosteric enhancers of the action of **adenosine** to activate the human-A1 **adenosine** receptor. None of the synthesized compds. appear to be more potent than I at a concentration of 10 μM. Most of the compds. increase the cAMP content of CHO cells expressing the human A1-**adenosine** receptor, indicating an

antagonist activity. Only two of the evaluated compds. appeared to be allosteric enhancers at high concentration (10 μM).
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1346847 CAPLUS
DOCUMENT NUMBER: 144:381438
TITLE: A3 **adenosine** receptors modulate hypoxia-inducible factor-1α expression in human A375 melanoma cells
AUTHOR(S): Merighi, Stefania; Benini, Annalisa; Mirandola, Prisco; Gessi, Stefania; Varani, Katia; **Leung, Edward**; MacLennan, Stephen; **Baraldi, Pier Giovanni**; **Borea, Pier Andrea**
CORPORATE SOURCE: Department of Clinical and Experimental Medicine-Pharmacology Unit, University of Ferrara, Ferrara, 44100, Italy
SOURCE: Neoplasia (Ann Arbor, MI, United States) (2005), 7(10), 894-903
CODEN: NEOPFL; ISSN: 1522-8002
PUBLISHER: Neoplasia Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hypoxia-inducible factor-1 (HIF-1) is a key regulator of genes crucial to many aspects of **cancer** biol. The purine nucleoside, **adenosine**, accumulates within many tissues under hypoxic conditions, including that of **tumors**. Because the levels of both HIF-1 and **adenosine** are elevated within the hypoxic environment of solid **tumors**, we investigated whether **adenosine** may regulate HIF-1. Here we show that, under hypoxic conditions (< 2% O2), **adenosine** upregulates HIF-1α protein expression in a dose-dependent and time-dependent manner, exclusively through the A3 receptor subtype. The response to **adenosine** was generated at the cell surface because the inhibition of A3 receptor expression, by using small interfering RNA, abolished nucleoside effects. A3 receptor stimulation in hypoxia also increases angiopoietin-2 (Ang-2) protein accumulation through the induction of HIF-1α. In particular, we found that A3 receptor stimulation activates p44/p42 and p38 mitogen-activated protein kinases, which are required for A3-induced increase of HIF-1α and Ang-2. Collectively, these results suggest a cooperation between hypoxic and **adenosine** signals that ultimately may lead to the increase in HIF-1-mediated effects in **cancer** cells.
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1261031 CAPLUS
DOCUMENT NUMBER: 144:5120
TITLE: Methods of diagnosing and prognosticating solid **tumors** and melanoma
INVENTOR(S): Liboni, Alberto; Gessi, Stefania; Maclennan, Steve; **Borea, Pier Andrea**; **Leung, Edward**
PATENT ASSIGNEE(S): King Pharmaceuticals Research & Development, Inc., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005113828	A1	20051201	WO 2005-US17495	20050513

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-571672P P 20040514

AB The invention relates to the diagnosis and prognosis of solid **tumors** and melanoma by detecting increased cellular levels of A3 receptors in tissue and/or leukocytes obtained from patients with **cancer** or patients at risk for developing **cancer**.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1162218 CAPLUS
DOCUMENT NUMBER: 144:32441
TITLE: Pharmacological characterization of novel **adenosine** ligands in recombinant and native human A2B receptors
AUTHOR(S): Varani, Katia; Gessi, Stefania; Merighi, Stefania; Vincenzi, Fabrizio; Cattabriga, Elena; Benini, Annalisa; Klotz, Karl-Norbert; **Baraldi, Pier Giovanni**; Tabrizi, Mojgan Aghazadeh; MacLennan, Stephen; **Leung, Edward**; **Borea, Pier Andrea**
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Ferrara, 44100, Italy
SOURCE: Biochemical Pharmacology (2005), 70(11), 1601-1612
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study was designed to evaluate the effects of novel and recognized compds. at human recombinant A2B **adenosine** receptors expressed in Chinese hamster ovary (hA2BCHO), in human embryonic kidney 293 (hA2BHEK-293) and at endogenous A2B receptors in human mast cells (HMC-1). Saturation binding expts. performed using the new high affinity A2B **adenosine** radioligand [3H]-N-benzo[1,3]dioxol-5-yl-2-[5-(2,6-dioxo-1,3-dipropyl-2,3,6,7-tetra hydro-1H-purin-8-yl)-1-methyl-1H-pyrazol-3-yloxy]-acetamide ([3H]-MRE 2029F20) revealed a single class of binding sites in hA2BCHO, hA2BHEK-293 and HMC-1 cells with K D (nM) of 1.65±0.18, 2.83±0.34, 2.62±0.27 and B max (fmol/mg protein) of 36±4, 475±50 and 128±15, resp. The pharmacol. profile of new compds., determined in inhibition binding expts. in hA2BHEK-293 cells using [3H]-MRE 2029F20, showed a rank order of potency typical of the A2B

receptors with K i values in the range 3.2-28 nM. In functional assays, recognized agonists and antagonists were studied by evaluating their capability to modulate the cAMP production in hA2BCHO and in HMC-1 cells. Novel compds. were able to decrease NECA-stimulated cAMP production in hA2BCHO and in HMC-1 cells showing a high potency. New compds. were also able to inhibit cAMP levels in the absence of NECA and in the presence of forskolin stimulation in hA2BCHO and in HMC-1 cells. In HEK-293 cells MRE 2029F20 reduced cAMP basal levels with an IC50 value of 2.9±0.3 nM. These results suggest that novel compds. are antagonists with an inverse agonist activity in recombinant and native human A2B receptors.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1159035 CAPLUS
DOCUMENT NUMBER: 144:88
TITLE: Recent improvements in the field of A3 **adenosine** receptor ligands
AUTHOR(S): **Baraldi, Pier Giovanni**; Fruttarolo, Francesca; Tabrizi, Mojgan Aghazadeh; Romagnoli, Romeo; Preti, Delia; Carrion, Maria Dora; Iaconinoto, Antonietta; **Borea, Pier Andrea**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy
SOURCE: Expert Opinion on Therapeutic Patents (2005), 15(11), 1507-1519
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. **Adenosine** regulates many physiol. functions via specific cell membrane receptors. To date, four **adenosine** receptor subtypes have been cloned, A1, A2A, A2B and A3, each of which exhibits a unique tissue distribution, ligand affinity and signal transduction mechanism. The pathophysiol. role of the A3 receptor might be very different from that of the A1 and A2A subtypes, in that A3 receptors could act as endogenous regulators under conditions of more severe challenge. To fully evaluate the biol. role of these receptors, subtype-selective agonists and antagonists with high affinity are required. Although most of the available ligands are only moderately selective for human A3 receptors, they have been useful probes to elucidate the function of this receptor subtype and have suggested a role for A3 receptors in inflammation, neurodegeneration, asthma and cardiac ischemia. Indeed, A3 receptor antagonists have been hypothesized to act as potential anti-asthmatic, anti-inflammatory or cerebroprotective agents. Moreover, A3 antagonists have been reported to induce apoptotic effects in some **tumor** cell lines at low concentration, whereas A3 **adenosine** agonists appear to exert dual and opposite effects, either cytoprotective or cytotoxic, depending on the cell type and the level of receptor activation.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:579741 CAPLUS
DOCUMENT NUMBER: 143:266861
TITLE: New 2-Arylpyrazolo[4,3-c]quinoline Derivatives as Potent and Selective Human **A3** **Adenosine** Receptor **Antagonists**

AUTHOR(S): **Baraldi, Pier Giovanni**; Tabrizi, Mojgan Aghazadeh; Preti, Delia; Bovero, Andrea; Fruttarolo, Francesca; Romagnoli, Romeo; Zaid, Naser Abdel; Moorman, Allan R.; Varani, Katia; **Borea, Pier Andrea**

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Dipartimento di Medicina Clinica e Sperimentale-Sezione di Farmacologia, Universita di Ferrara, Ferrara, 44100, Italy

SOURCE: Journal of Medicinal Chemistry (2005), 48(15), 5001-5008
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis and biol. evaluation of a new class of 2-phenyl-2,5-di(hydro)pyrazolo[4,3-c]quinolin-4-one derivs. as **A3 adenosine** receptor **antagonists** was reported. A new route based on the Kira-Vilsmeier reaction for the synthesis of this class of compds. was designed. Some of the synthesized compds. showed A3 **adenosine** receptor affinity in the nanomolar range and good selectivity as evaluated in radioligand binding assays at human (h) A1, A2A, A2B, and A3 **adenosine** receptor subtypes. Several substituents on the 2-Ph ring were introduced. In particular substitution at the 4-position by Me, methoxy, and chlorine gave optimal activity and selectivity. In conclusion, the 2-phenyl-2,5-dihydro-pyrazolo[4,3-c]quinolin-4-one derivs. described herein represent a new family of in vitro selective **antagonists** for the **adenosine A3** receptor. Selective **adenosine A3** receptor **antagonists** are potential antiasthmatic, antiinflammatory, or cerebroprotective agents (no data).

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:538828 CAPLUS

DOCUMENT NUMBER: 143:211759

TITLE: New Pyrrolo[2,1-f]purine-2,4-dione and Imidazo[2,1-f]purine-2,4-dione Derivatives as Potent and Selective Human **A3 Adenosine** Receptor **Antagonists**

AUTHOR(S): **Baraldi, Pier Giovanni**; Preti, Delia; Tabrizi, Mojgan Aghazadeh; Fruttarolo, Francesca; Romagnoli, Romeo; Zaid, Naser Abdel; Moorman, Allan R.; Merighi, Stefania; Varani, Katia; **Borea, Pier Andrea**

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche and Dipartimento di Medicina Clinica e Sperimentale-Sezione di Farmacologia, Universita di Ferrara, Ferrara, 44100, Italy

SOURCE: Journal of Medicinal Chemistry (2005), 48(14), 4697-4701
CODEN: JMCMAR; ISSN: 0022-2623

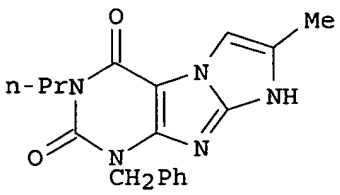
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:211759

GI



I

AB Compds. presenting an addnl. fused ring on the xanthine nucleus have been reported to exhibit antagonistic activity with various levels of affinity and selectivity toward the four **adenosine** receptors subtypes A1, A2A, A2B, and A3. This paper reports synthesis and biol. evaluation of new 1-benzyl-3-propyl-1H,6H-pyrrolo[2,1-f]purine-2,4-diones and 1-benzyl-3-propyl-1H,8H-imidazo[2,1-f]purine-2,4-diones, among which we identified potent and selective **A3 adenosine** receptors **antagonists**. In particular, 1-benzyl-7-methyl-3-propyl-1H,8H-imidazo[2,1-f]purine-2,4-dione (I) shows a Ki (hA3) value from binding assay of 0.8 nM.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:495122 CAPLUS

DOCUMENT NUMBER: 143:146976

TITLE: Expression, pharmacological profile, and functional coupling of A2B receptors in a recombinant system and in peripheral blood cells using a novel selective antagonist radioligand, [3H]MRE 2029-F20

AUTHOR(S): Gessi, Stefania; Varani, Katia; Merighi, Stefania; Cattabriga, Elena; Pancaldi, Cecilia; Szabadkai, Youri; Rizzuto, Rosario; Klotz, Karl-Norbert; **Leung, Edward**; Mac Lennan, Stephen; **Baraldi, Pier Giovanni**; **Borea, Pier Andrea**

CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Italy

SOURCE: Molecular Pharmacology (2005), 67(6), 2137-2147
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In this study, we compared the pharmacol. and biochem. characteristics of A2B **adenosine** receptors in recombinant (hA2BHEK293 cells) and native cells (neutrophils, lymphocytes) by using a new potent 8-pyrazole xanthine derivative, [3H]N-benzo[1,3]dioxol-5-yl-2-[5-(1,3-dipropyl-2,6-dioxo-2,3,6,7- tetrahydro-1H-purin-8-yl)-1-methyl-1H-pyrazol-3-yl-oxy-acetamide] ([3H]MRE 2029-F20); that has high affinity and selectivity for hA2B vs. hA1, hA2A, and hA3 subtypes. [3H]MRE 2029-F20 bound specifically to the hA2B receptor stably transfected in human embryonic kidney (HEK) 293 cells with KD of 2.8±0.2 nM and Bmax of 450±42 fmol/mg of protein. Saturation expts. of [3H]MRE 2029-F20 binding in human neutrophils and lymphocytes detected a single high-affinity binding site with KD values of 2.4±0.5 and 2.7±0.7 nM, resp., and Bmax values of 79±10 and 54±8 fmol/mg

of protein, resp., in agreement with real-time reverse transcription polymerase chain reaction studies showing the presence of A2B mRNA. The rank order of potency of typical **adenosine** ligands with recombinant hA2B receptors was consistent with that typically found for interactions with the A2B subtype and was also similar in peripheral blood cells. 5'-N-Ethylcarboxamidoadenosine stimulated cAMP accumulation in both hA2BHEK293 and native cells, whereas phospholipase C activation was observed in recombinant receptors and endogenous subtypes expressed in neutrophils but not in lymphocytes. MRE 2029-F20 was revealed to be a potent antagonist in counteracting the agonist effect in both signal transduction pathways. In conclusion, [3H]MRE 2029-F20 is a selective and high-affinity radioligand for the hA2B **adenosine** subtype and may be used to quantify A2B endogenous receptors. In this work, we demonstrated their presence and functional coupling in neutrophils and lymphocytes that play a role in inflammatory processes in which A2B receptors may be involved.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:452251 CAPLUS
DOCUMENT NUMBER: 143:165745
TITLE: Pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine ligands, new tools to characterize A3 **adenosine** receptors in human **tumor** cell lines
AUTHOR(S): **Baraldi, Pier Giovanni**; Tabrizi, Mojgan Aghazadeh; Romagnoli, Romeo; Fruttarolo, Francesca; Merighi, Stefania; Varani, Katia; Gessi, Stefania; **Borea, Pier Andrea**
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Ferrara, Italy
SOURCE: Current Medicinal Chemistry (2005), 12(11), 1319-1329
CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Increased concns. of extracellular **adenosine** are reached in ischemic or inflamed tissues but have also been detected inside **tumoral** masses. If this finding may account for an important role of **adenosine** in the pathogenesis of **tumors** remains to be determined in view of its contradictory effects on cell survival and proliferation. In particular, **adenosine** was found to exert its effects on proliferation and on cell death mainly through the A3 **adenosine** receptor. Therefore, a complete pharmacol. characterization of the subtype and number of the expressed A3 **adenosine** receptors is necessary for the elucidation of the role of **adenosine** via A3 receptors in a specific cell subtype. The lack of potent and selective radiolabeled A3 receptor antagonists has been, in the past, the major obstacle in the characterization of structure, function and regulation of this **adenosine** receptor subtype. Recently, our group has identified a series of substituted pyrazolotriazolopyrimidine derivs. as potent and selective **antagonists** to human **A3 adenosine** receptors. The most recent results obtained in this field are summarized in the present review. Furthermore, the review reports the results of the biochem. and pharmacol. characterization of A3 receptors in different human **tumor** cell lines and the multiple A3 receptor-sustained ways that could prime **tumor** development.

REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:283498 CAPLUS
DOCUMENT NUMBER: 142:336591
TITLE: Preparation of sulfonamido nucleosides as human **adenosine** A3 receptor agonists and antitumor agents
INVENTOR(S): **Baraldi, Pier Giovanni**; Moorman, Allan R.; **Borea, Pier A.**
PATENT ASSIGNEE(S): King Pharmaceuticals Research & Development, Inc., USA
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005028489	A2	20050331	WO 2004-US30514	20040917
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004274475	A1	20050331	AU 2004-274475	20040917
CA 2537094	AA	20050331	CA 2004-2537094	20040917
US 2005250729	A1	20051110	US 2004-944245	20040917
EP 1668020	A2	20060614	EP 2004-788819	20040917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

PRIORITY APPLN. INFO.: US 2003-504579P P 20030918
WO 2004-US30514 W 20040917

OTHER SOURCE(S): MARPAT 142:336591
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention realizes that a series of sulfonamido derivs. I, wherein wherein Ar is an aryl group; and R and R1 are independently H, alkyl, aryl, heteroaryl, alkenyl, cycloalkenyl, cycloalkyl, alkoxy, alkynyl, and where taken together R and R1 may form a or carbocyclic or heterocyclic fused ring system which includes both alicyclic and aromatic structures with a conserved uronamide group at the 5' position provide superior A3 receptor affinity as well as selectivity. These new **adenosine** agonists are sulfonamido derivs. N-substituted with aliphatic groups (cyclic or linear) or aromatic radicals. Mediation of the A3 receptor has been found to induce behavioral depression and protect against cerebral ischemia, and

to induce apoptosis in HL-60 human leukemia cells. The A3 **adenosine** receptor is known to mediate many processes, such as inflammation, hypotension, and mast cell deregulation. These compds. can be used to treat **cancer**. This particularly includes **cancers** that express elevated levels of A3 receptors. This would include, but not be limited to, ovarian **cancer**, breast **cancer**, colon **cancer**, and melanoma. Thus, nucleoside II was prepared and tested in vitro as **adenosine** A3 receptor agonist and antitumor agent.

L32 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1106821 CAPLUS
DOCUMENT NUMBER: 142:147845
TITLE: Combined Target-Based and Ligand-Based Drug Design Approach as a Tool To Define a Novel 3D-Pharmacophore Model of Human **A3 Adenosine** Receptor **Antagonists**: Pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine Derivatives as a Key Study
AUTHOR(S): Moro, Stefano; Braiuca, Paolo; Deflorian, Francesca; Ferrari, Cristina; Pastorin, Giorgia; Cacciari, Barbara; **Baraldi, Pier Giovanni**; Varani, Katia; **Borea, Pier Andrea**; Spalluto, Giampiero
CORPORATE SOURCE: Molecular Modeling Section, Dipartimento di Scienze Farmaceutiche, Universita di Padova, Padua, I-35131, Italy
SOURCE: Journal of Medicinal Chemistry (2005), 48(1), 152-162
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:147845
AB A combined target-based and ligand-based drug design approach has been carried out to define a novel pharmacophore model of the human A3 receptor antagonists. High throughput mol. docking and comparative mol. field anal. (CoMFA) have been used in tandem to assemble a new target based pharmacophore model. In parallel, to provide more accurate information about the putative binding site of these A3 inhibitors, a rhodopsin-based model of the human A3 receptor was built and a novel Y-shape binding motif has been proposed. Docking-based structure superimposition has been used to perform a quant. study of the structure-activity relationships for binding of these pyrazolo-triazolo-pyrimidines to **adenosine** A3 receptor using CoMFA. Both steric and the electrostatic contour plots obtained from the CoMFA anal. nicely fit on the hypothetical binding site obtained by mol. docking. On the basis of the combined hypothesis, we have designed, synthesized, and tested 17 new derivs. Consistently, the predicted Ki values were very close to the exptl. values.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 16 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:738048 CAPLUS
DOCUMENT NUMBER: 141:409145
TITLE: Elevated expression of A3 **adenosine** receptors in human colorectal **cancer** is reflected in peripheral blood cells
AUTHOR(S): Gessi, Stefania; Cattabriga, Elena; Avitabile, Arianna; Gafa', Roberta; Lanza, Giovanni; Cavazzini, Luigi; Bianchi, Nicoletta; Gambari, Roberto; Feo,

Carlo; Liboni, Alberto; Gullini, Sergio; **Leung, Edward**; Mac-Lennan, Stephen; **Borea, Pier Andrea**
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, University of Ferrara, Ferrara, Italy
SOURCE: Clinical Cancer Research (2004), 10(17), 5895-5901
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Adenosine** is a ubiquitous nucleoside that accumulates at high levels in hypoxic regions of solid **tumors**, and A3 **adenosine** receptors have been recently demonstrated to play a pivotal role in the **adenosine**-mediated inhibition of **tumor** cell proliferation. In the present work, the authors addressed the question of the putative relevance of A3 subtypes in colorectal adenocarcinomas. Seventy-three paired samples of **tumor** and surrounding peritumoral normal mucosa at a distance of 2 and 10 cm from the **tumor** and blood samples obtained from a cohort of 30 patients with colorectal **cancer** were investigated to determine the presence of A3 receptors by means of binding, immunocytochem., and real-time reverse transcription-polymerase chain reaction studies. As measured by receptor binding assays, the d. of A3 receptor was higher in colon carcinomas as compared with normal mucosa originating from the same individuals ($P < 0.05$). Overexpression of A3 receptors at the protein level was confirmed by immunohistochem. studies, whereas no changes in A3 mRNA accumulation in **tumors** as compared with the corresponding normal tissue were revealed. The overexpression of A3 receptors in **tumors** was reflected in peripheral blood cells, where the d. was approx. 3-fold higher compared with healthy subjects ($P < 0.01$). In a cohort of 10 patients studied longitudinally, expression of A3 receptors in circulating blood cells returned to normal after surgical resection for colorectal **cancer**. This study provides the first evidence that A3 receptor plays a role in colon **tumorigenesis** and, more importantly, can potentially be used as a diagnostic marker or a therapeutic target for colon **cancer**.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:2642 CAPLUS
DOCUMENT NUMBER: 140:70996
TITLE: Enhancing treatment of **MDR cancer** with **adenosine A3 antagonists**
INVENTOR(S): **Borea, Pier Andrea**; **Baraldi, Pier Giovanni**; **Chen, Shih-Fong**; **Leung, Edward**
PATENT ASSIGNEE(S): King Pharmaceuticals Research & Development, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000237	A2	20031231	WO 2003-US20118	20030624

WO 2004000237 A3 20040226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2464539 AA 20031231 CA 2003-2464539 20030624
AU 2003245693 A1 20040106 AU 2003-245693 20030624
US 2004067932 A1 20040408 US 2003-603406 20030624
BR 2003005106 A 20040928 BR 2003-5106 20030624
EP 1515719 A2 20050323 EP 2003-739312 20030624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2005530858 T2 20051013 JP 2004-530977 20030624
PRIORITY APPLN. INFO.: US 2002-391009P P 20020624
US 2002-394395P P 20020708
WO 2003-US20118 W 20030624

OTHER SOURCE(S): MARPAT 140:70996

AB The invention discloses the use of high affinity **adenosine A3** receptor **antagonists** for enhancing chemotherapeutic treatment of **cancers** expressing **adenosine** A3 receptors and **cancers** expressing P-glycoprotein or MRP. In preferred embodiments, **adenosine A3** receptor **antagonists** are administered before or during administration of a taxane family, vinca alkaloid, camptothecin or antibiotic chemotherapeutic agent.

L32 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:2631 CAPLUS
DOCUMENT NUMBER: 140:70994
TITLE: Enhancing treatment of **MDR cancer** with **adenosine A3 antagonists**
INVENTOR(S): **Borea, Pier Andrea; Baraldi, Pier Giovanni; Chen, Shih-Fong; Leung, Edward**
PATENT ASSIGNEE(S): King Pharmaceuticals Research & Development, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000224	A2	20031231	WO 2003-US19687	20030620
WO 2004000224	A3	20040408		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003251595	A1	20040106	AU 2003-251595	20030620
US 2005119289	A1	20050602	US 2003-600116	20030620
ZA 2004001450	A	20050310	ZA 2004-1450	20040224
PRIORITY APPLN. INFO.:			US 2002-391009P P	20020624
			WO 2003-US19687 W	20030620

OTHER SOURCE(S): MARPAT 140:70994

AB The invention discloses the use of high affinity **adenosine A3** receptor **antagonists** for enhancing chemotherapeutic treatment of **cancers** expressing **adenosine** A3 receptors and **cancers** expressing P-glycoprotein or MRP. In preferred embodiments, **adenosine A3** receptor **antagonists** are administered before or during administration of a taxane family, vinca alkaloid, camptothecin or antibiotic chemotherapeutic agent.

L32 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:971891 CAPLUS
DOCUMENT NUMBER: 140:13098
TITLE: Pharmaceutically active compounds having a tricyclic pyrazolotriazolopyrimidine ring structure and methods of use
INVENTOR(S): **Baraldi, Pier Giovanni**; **Borea, Pier Andrea**
PATENT ASSIGNEE(S): King Pharmaceuticals Research & Development, Inc., USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101455	A2	20031211	WO 2003-US17313	20030530
WO 2003101455	A3	20040521		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2454654	AA	20031211	CA 2003-2454654	20030530
AU 2003245380	A1	20031219	AU 2003-245380	20030530
US 2004039004	A1	20040226	US 2003-452788	20030530
BR 2003004963	A	20040928	BR 2003-4963	20030530
EP 1549319	A2	20050706	EP 2003-739019	20030530

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2005527635	T2	20050915	JP 2004-508812	20030530
ZA 2004000784	A	20050503	ZA 2004-784	20040130
PRIORITY APPLN. INFO.:			US 2002-384809P P	20020530
			WO 2003-US17313 W	20030530

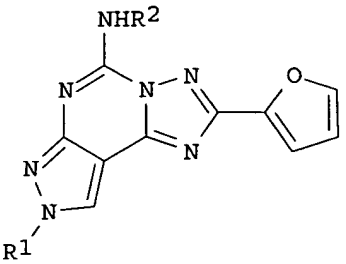
OTHER SOURCE(S): MARPAT 140:13098

AB Tricyclic pyrazolotriazolopyrimidines which possess antagonistic activity for **adenosine** receptors may be useful for modulating biol. function in the nervous, cardiovascular, renal, respiratory and immune systems. General synthetic schemes and examples of formulations for the compds. are presented.

L32 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:787328 CAPLUS
DOCUMENT NUMBER: 140:101
TITLE: A glance at **adenosine** receptors: novel target for antitumor therapy
AUTHOR(S): Merighi, Stefania; Mirandola, Prisco; Varani, Katia; Gessi, Stefania; **Leung, Edward**; **Baraldi, Pier Giovanni**; Tabrizi, Mojgan Aghazadeh; **Borea, Pier Andrea**
CORPORATE SOURCE: Pharmacology Unit, Department of Clinical and Experimental Medicine, Ferrara, 44100, Italy
SOURCE: Pharmacology & Therapeutics (2003), 100(1), 31-48
CODEN: PHTHDT; ISSN: 0163-7258
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with refs. **Adenosine** can be released from a variety of cells throughout the body, as the result of increased metabolic rates, in concns. that can have a profound impact on the vasculature, immunoescaping, and **growth** of **tumor** masses. It is recognized that the concns. of this nucleoside are increased in **cancer** tissues. Therefore, it is not surprising that **adenosine** has been shown to be a crucial factor in determining the cell progression pathway, either during apoptosis or during cytostatic state. From the perspective of **cancer**, the most important question then may be "Can activation and/or blockade of the pathways downstream of the **adenosine** receptor contribute to **tumor** development". Rigorous examns. of the role of **adenosine** in in vivo and in vitro systems need to be investigated. The present review therefore proposes multiple **adenosine**-sustained ways that could prime **tumor** development together with the critical combinatorial role played by **adenosine** receptors in taking a choice between proliferation and death. This review proposes that **adenosine** acts as a potent regulator of normal and **tumor** cell **growth**. It is hypothesized that this effect is dependent on extracellular **adenosine** concns., cell surface expression of different **adenosine** receptor subtypes, and signal transduction mechanisms activated following the binding of specific agonists. We venture to suggest that the clarification of the role of **adenosine** and its receptors in **cancer** development may hold great promise for the treatment of chemotherapy in patients affected by malignancies.
REFERENCE COUNT: 156 THERE ARE 156 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:686358 CAPLUS
DOCUMENT NUMBER: 140:111366
TITLE: New strategies for the synthesis of **A3** **adenosine** receptor **antagonists**
AUTHOR(S): **Baraldi, Pier Giovanni**; Bovero, Andrea; Fruttarolo, Francesca; Romagnoli, Romeo; Tabrizi, Mojgan Aghazadeh; Preti, Delia; Varani, Katia;

Borea, Pier Andrea; Moorman, Allan R.
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy
SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(19), 4161-4169
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:111366
GI



I

AB New **A3 adenosine** receptor **antagonists** I [R1 = HO(CH2)2, (EtO)2CHCH2, HO2CCH2, etc.; R2 = H, PhNHCO, 3-ClC6H4NHCO] were synthesized and tested at human **adenosine** receptor subtypes. An advanced synthetic strategy permitted us to obtain a large amount of the key intermediate I (R1 = R2 = H) that was then submitted to alkylation procedures in order to obtain I [R1 = HO(CH2)2, (EtO)2CHCH2, Me3CO2CCH2, etc.; R2 = H]. The latter were then functionalized into ureas at the 5-position to evaluate their affinity and selectivity vs. hA3 **adenosine** receptor subtype; in particular, I [R1 = PhCH2O(CH2)2, HO(CH2)2; R2 = PhNHCO] displayed a value of affinity of 4.9 and 1.3 nM, resp. Starting from I (R1 = R2 = H), the synthetic methodologies employed allowed to perform a rapid and a convenient divergent synthesis. This method could be used as a general procedure for the design of novel **A3 adenosine** receptor **antagonists** without the difficulty of separating the N8-substituted pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidines from the corresponding N7-isomers.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:669201 CAPLUS
DOCUMENT NUMBER: 140:138838
TITLE: Pyrazolotriazolopyrimidine derivatives sensitize melanoma cells to the chemotherapeutic drugs: taxol and vindesine
AUTHOR(S): Merighi, Stefania; Mirandola, Prisco; Varani, Katia; Gessi, Stefania; Capitani, Silvano; **Leung, Edward**; **Baraldi, Pier Giovanni**; Tabrizi, Mojgan Aghazadeh; **Borea, Pier Andrea**
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Ferrara, 44100, Italy
SOURCE: Biochemical Pharmacology (2003), 66(5), 739-748
CODEN: BCPCA6; ISSN: 0006-2952

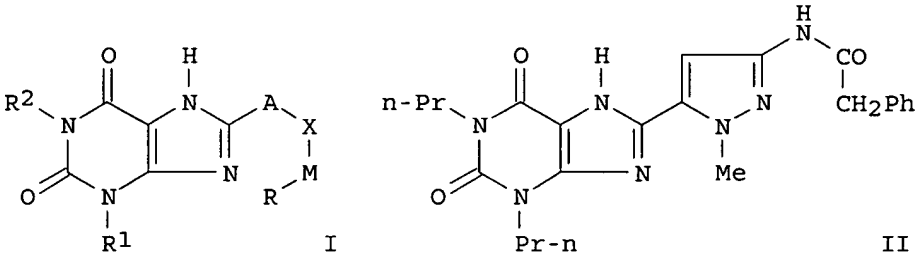
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this study, we have evaluated the "in vitro" modulatory activity of a series of pyrazolotriazolopyrimidine derivs. (PTP-d) in sensitizing malignant melanoma cells to the chemotherapeutic drugs: taxol and vindesine. To that end, we have described the impact of chemotherapeutic agents on the cell cycle and on the induction of apoptosis when used alone or in combination with PTP-d. We have demonstrated that four PTP-d reduced chemotherapeutic drugs EC50 doses of the G2/M accumulation with an average of 1.7-fold for taxol and 9.5-fold for vindesine when challenged on A375 human melanoma cell line. This sensitization activity was also confirmed by analyzing the apoptosis degree induced by the chemotherapeutic drugs. Interestingly, PTP-d had no effects on the response to cytotoxic agents by skin-derived human keratinocyte cells, NCTC 2544. Therefore, we have investigated the signaling pathway sustaining the sensitizing effect of PTP-d, providing functional evidence that active compds. are able to inhibit multidrug resistance-associated ATP-binding cassette drug transporter. These results suggested that PTP-d hold great promise for the treatment of multidrug resistance in **cancers**, leading to potential new therapies for melanoma.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:610209 CAPLUS
DOCUMENT NUMBER: 139:164659
TITLE: Preparation of 8-heteroarylxanthine **adenosine** A2B receptor antagonists for use in pharmaceutical compositions
INVENTOR(S): **Baraldi, Pier Giovanni; Borea, Pier A.**
PATENT ASSIGNEE(S): King Pharmaceuticals Research and Development, Inc., USA
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063800	A2	20030807	WO 2003-US3224	20030203
WO 2003063800	A3	20031224		
WO 2003063800	C1	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2443023	AA	20030807	CA 2003-2443023	20030203
US 2003207879	A1	20031106	US 2003-357865	20030203
EP 1469856	A2	20041027	EP 2003-710831	20030203

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003002965	A	20050209	BR 2003-2965		20030203
JP 2005516975	T2	20050609	JP 2003-563496		20030203
ZA 2003007672	A	20050504	ZA 2003-7672		20031001
PRIORITY APPLN. INFO.:			US 2002-353317P	P	20020201
			WO 2003-US3224	W	20030203

OTHER SOURCE(S): MARPAT 139:164659
GI



I II

AB 8-Heteroarylxanthines, such as I [R = aryl, heteroaryl, amino, carboxy, NO2, OH, etc; R1, R2 = H, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl; R3 = H, alkyl, alkenyl, alkynyl; A = bond, alkylene, alkenylene, alkynylene; M = bond, carbonyl containing alkylene, alkenylene, alkynylene, heteroalkylene, heteroalkenylene, heteroalkynylene, etc.; X = 5 or 6 membered heterocyclic ring], were prepared for therapeutic use as **adenosine** A2B receptor antagonists. These 8-heteroarylxanthines are useful for treatment of autoimmune, inflammatory, and vascular diseases which are mediated by **adenosine** A2B receptors such as, retinal vascular diseases, acute inflammatory diseases involving degranulation of mast cells including asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, allergic rhinitis, allergic dermatitis and bee sting, impaired sensitivity to insulin including type 2 diabetes or non-insulin dependent diabetes, pre-diabetic state, impaired glucose tolerance, diseases in which angiogenesis is a key component of pathogenesis, including solid **tumors** and angiogenic retinopathy, apnea of pre-term infants, myocardial reperfusion injury, inflammatory bowel disease, multiple sclerosis, and lupus erythematosis. Thus, II was prepared via a cyclocondensation reaction of 1-methyl-3-(benzyloxycarbonylamino)pyrazole-5-carboxylic acid with 1,3-dipropyl-5,6-diaminouracil using EDCI in MeOH to form the pyrazolylxanthine moiety and subsequent N-acylation with phenylacetic acid using thionyl chloride and Et3N in CH2Cl2. The prepared xanthines were tested for affinity to human A1, A2A, A2B, and A3 **adenosine** receptors.

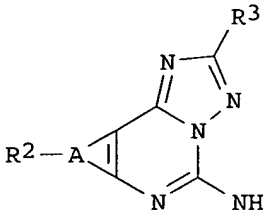
L32 ANSWER 24 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:590829 CAPLUS
DOCUMENT NUMBER: 139:133584
TITLE: Preparation of pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidines and analogs as **adenosine** A3 receptor modulators for therapeutic and diagnostic use
INVENTOR(S): **Baraldi, Pier Giovanni; Borea, Pier Andrea**
PATENT ASSIGNEE(S): King Pharmaceuticuals Research & Development, Inc., Italy

SOURCE: U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of U.S. 6,407,236.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

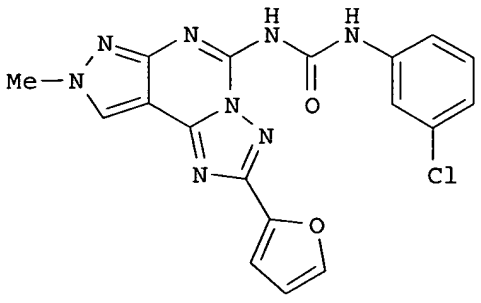
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003144266	A1	20030731	US 2002-134219	20020426
US 6921825	B2	20050726		
US 6448253	B1	20020910	US 1998-154435	19980916
US 6407236	B1	20020618	US 1999-379300	19990823
AU 2002305386	A1	20031111	AU 2002-305386	20020506
CA 2451081	AA	20031120	CA 2002-2451081	20020506
WO 2003095457	A1	20031120	WO 2002-US14191	20020506
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
BR 2002010720	A	20040720	BR 2002-10720	20020506
EP 1499614	A1	20050126	EP 2002-734202	20020506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
ZA 200309907	A	20050322	ZA 2003-9907	20020506
JP 2006510574	T2	20060330	JP 2004-503471	20020506
US 2006040959	A1	20060223	US 2005-169311	20050627

PRIORITY APPLN. INFO.:		
US 1998-154435	A2	19980916
US 1999-379300	A2	19990823
US 2002-134219	A	20020426
WO 2002-US14191	W	20020506

OTHER SOURCE(S): MARPAT 139:133584
GI



I



II

AB Title compds. I [wherein A = imidazole, pyrazole, or triazole; R = CXR1,

CXN(R1)2, CXOR1, CXSR1, SOnR1, SOnSR1, or SOnN(R1)2; R1 = H, (hetero)aryl, heterocyclyl, alkanoyl, or (un)substituted alkyl, alkenyl, or alkynyl; or N(R1)2 = azetidinyl or 5-6 membered heterocyclyl; R2 = H or (un)substituted alkyl, alkenyl, aralkyl, or (hetero)aryl; R3 = (un)substituted (benzo)furanyl, (benzo)pyrrolyl, or (benzo)thiophenyl; X = O, S, or NR1; n = 0-2; or pharmaceutically acceptable salts thereof] were prepared as selective A3 **adenosine** receptor agonists. Thus, 3-amino-1H-pyrazole-4-carbonitrile was methylated, treated with tri-Et orthoformate to give the imidate, and cyclized with 2-furoic acid hydrazide to give 8-methyl-2-(2-furyl)pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine (45%). Amination (53%) and addition of 3-chlorophenyl isocyanate (98%) afforded II, which exhibited binding affinity at the A1, A2, and A3 receptors with Ki values of 5,045 nM, >10,1000 nM, and 0.22 nM, resp. I are useful for the treatment disorders caused by excessive activation of the A3 receptor, such as hypertension, inflammation, mast cell degranulation, cardiac hypoxia, allergic disease, and for protection against cerebral ischemia (no data). In addition, I are useful in diagnostic applications to determine the relative binding of other compds. to the A3 receptor. For instance, the compds. can be labeled, for example with fluorescent or radiolabels, and the labels used in vivo or in vitro to determine the presence of **tumor** cells which possess a high concentration of **adenosine** A3 receptors.

REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

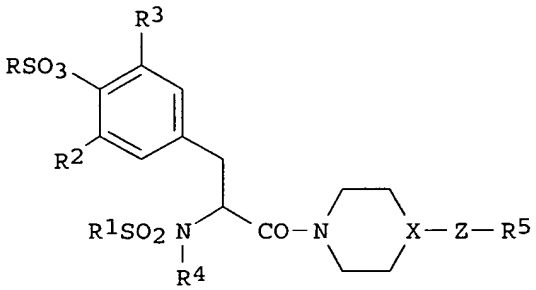
L32 ANSWER 25 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:570819 CAPLUS
DOCUMENT NUMBER: 139:117684
TITLE: Preparation of tyrosyl derivatives as P2X7 receptor modulators
INVENTOR(S): **Baraldi, Pier Giovanni; Borea, Pier A.**
PATENT ASSIGNEE(S): King Pharmaceuticals Research and Development, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059353	A1	20030724	WO 2002-US41385	20021223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2471562	AA	20030724	CA 2002-2471562	20021223
AU 2002361864	A1	20030730	AU 2002-361864	20021223
US 2003181452	A1	20030925	US 2002-329094	20021223
BR 2002015288	A	20041221	BR 2002-15288	20021223
EP 1487449	A1	20041222	EP 2002-797493	20021223

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

CN 1617725	A	20050518	CN 2002-827812		20021223
JP 2005517684	T2	20050616	JP 2003-559515		20021223
ZA 2004005327	A	20050705	ZA 2004-5327		20040705
PRIORITY APPLN. INFO.:			US 2001-342977P	P	20011221
			WO 2002-US41385	W	20021223

OTHER SOURCE(S): MARPAT 139:117684
GI



I

AB Tyrosyl derivs., e.g, I [R, R1 = (6/7/8-aza)-1-naphthyl; R2, R3 = H, D, T, or halo; R4 = H, Me; X = CH, N; Z = CO, (CH2)0-4; R5 = (un)substituted (2/6-aza)phenyl], are disclosed as modulators of the P2X7 receptor. Thus, 1-[(S)-N,O-bis(isoquinolinesulfonyl)-N-methyltyrosyl]-4-(4-nitrophenyl)piperazine was prepared by amidation of N-(tert-butoxycarbonyl)-N-methyl-L-tyrosine with 1-(4-nitrophenyl)piperazine, followed by O-sulfonylation, deprotection and N-sulfonylation, and showed IC50 = 5.76 nM P2X7 antagonist activity.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2003:466174 CAPLUS
DOCUMENT NUMBER:	139:131495
TITLE:	**Adenosine** receptors and human melanoma
AUTHOR(S):	Merighi, Stefania; **Baraldi, Pier Giovanni**; Gessi, Stefania; Iannotta, Valeria; Klotz, Karl-Norbert; **Leung, Edward**; Mirandola, Prisco; Tabrizi, Mojgan Aghazadeh; Varani, Katia; **Borea, Pier Andrea**
CORPORATE SOURCE:	Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Ferrara, Italy
SOURCE:	Drug Development Research (2003), 58(4), 377-385 CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER:	Wiley-Liss, Inc.
DOCUMENT TYPE:	Journal; General Review
LANGUAGE:	English

AB A review. Increased concns. of extracellular **adenosine** are reached in ischemic or inflamed tissues but have also been detected inside **tumoral** masses. This latter finding may account for an important role of **adenosine** in the pathogenesis of **tumors** and its contradictory effects on cell survival and proliferation remain to be

reconciled with the presence of specific **adenosine** receptor subtypes. This article reviews the pharmacol. and biochem. characterization of **adenosine** receptors in the human malignant melanoma A375 cell line and the functional significance of their presence in a **tumor** cell type. The authors show that **adenosine** improves cell proliferation via A2A receptors while it arrests the cells at G1/G0 cell cycle phase through A3 stimulation. Furthermore, **adenosine** triggers a survival signal via A3 receptor stimulation while it simultaneously promotes cell death via A2A receptor activation, inducing a signaling pathway that involves protein kinase C (PKC) and mitogen-activated protein kinases (MAPKs).

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:466168 CAPLUS
DOCUMENT NUMBER: 139:301093
TITLE: Recent developments in the field of **A3 adenosine** receptor **antagonists**
AUTHOR(S): **Baraldi, Pier Giovanni**; Tabrizi, Mojgan Aghazadeh; Fruttarolo, Francesca; Bovero, Andrea; Avitabile, Barbara; Preti, Delia; Romagnoli, Romeo; Merighi, Stefania; Gessi, Stefania; Varani, Katia; **Borea, Pier Andrea**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, Italy
SOURCE: Drug Development Research (2003), 58(4), 315-329 CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review of studies done by the authors and others. **Adenosine** is an endogenous modulator of a large variety of physiol. functions through the interaction with specific cell membrane G-protein-coupled receptors classified as A1, A2A, A2B, and A3. Activation of A3 receptors has been shown to stimulate phospholipase C and to inhibit adenylate cyclase. A3 agonists also cause stimulation of phospholipase D and the release of inflammatory mediators, such as histamine from mast cells, which are responsible for inflammation and hypotension. For these reasons, the clin. use of **A3 adenosine** receptors **antagonists** for the treatment of asthma and inflammatory disease has been suggested. Recent studies also indicated a possible employment of these derivs. as antitumor agents. Different classes of polyheterocyclic compds. have been identified as potent A3 antagonists. Herein, we report our past and recent results in the development of tricyclic A3 selective antagonists. The pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine nucleus has especially been investigated by our group.

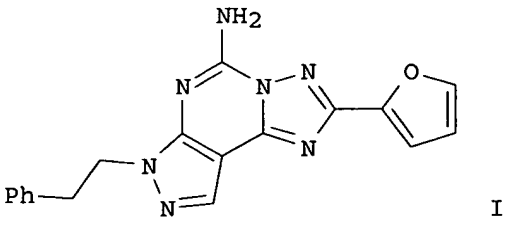
Our interests were focused on the effects of substitution of the Ph ring of the arylcarbamoyl moiety at N5 position and of substituents at C9 and/or at N8 pyrazole nitrogen. These studies allowed us to obtain a large variety of compds. which showed affinities in the nanomolar range with human A3 **adenosine** receptors with a high degree of selectivity vs. all other receptors subtypes. Thanks to the introduction of alkylating groups at p-position of the N5-phenylcarbamoyl chain, we succeeded in realizing potent irreversible **A3 adenosine antagonists**. Finally, the replacement of the Ph nucleus of carbamoyl function with a pyridine ring conferred water solubility to the corresponding derivs., which are also characterized by high levels of A3

affinity and selectivity.
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:364659 CAPLUS
DOCUMENT NUMBER: 139:206865
TITLE: Recent developments in the field of A2A and **A3** **adenosine** receptor **antagonists**
AUTHOR(S): **Baraldi, Pier Giovanni**; Tabrizi, Mojgan Aghazadeh; Bovero, Andrea; Avitabile, Barbara; Preti, Delia; Fruttarolo, Francesca; Romagnoli, Romeo; Varani, Katia; **Borea, Pier Andrea**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy
SOURCE: European Journal of Medicinal Chemistry (2003), 38(4), 367-382
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. In the last years **adenosine** receptors have been extensively studied, and mainly at present the importance of A2A and A3 **adenosine** receptors is understood. A2A selective **adenosine** receptors antagonists are promising new drugs for the treatment of Parkinson's disease, while **A3** selective **adenosine** receptors **antagonists** have been postulated as novel anti-inflammatory and antiallergic agents; recent studies also indicated a possible employment of these derivs. as antitumor agents. Lately different classes of compds. have been identified as potent A2A and A3 antagonists. In this article we report the past and present efforts which led to development of more potent and selective A2A and A3 antagonists. This research group has mainly worked on the pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine nucleus both as A2A and A3 antagonists, aiming to improve the affinity, selectivity and the hydrophilic profile. In fact, several compds. endowed with high affinity and selectivity vs. A2A **adenosine** receptors or A3 **adenosine** receptors were synthesized. .
REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:151162 CAPLUS
DOCUMENT NUMBER: 138:321211
TITLE: Design, Synthesis, and Biological Evaluation of C9- and C2-Substituted Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines as New A2A and **A3** **Adenosine** Receptor **Antagonists**
AUTHOR(S): **Baraldi, Pier Giovanni**; Fruttarolo, Francesca; Tabrizi, Mojgan Aghazadeh; Preti, Delia; Romagnoli, Romeo; El-Kashef, Hussein; Moorman, Allan; Varani, Katia; Gessi, Stefania; Merighi, Stefania; **Borea, Pier Andrea**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche and Dipartimento di Medicina Clinica e Sperimentale-Sezione di Farmacologia, Universita di Ferrara, Ferrara, 44100, Italy
SOURCE: Journal of Medicinal Chemistry (2003), 46(7), 1229-1241

CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:321211
GI



I

AB Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines such as I are prepared as selective **adenosine** A2a and **A3** receptor **antagonists**. Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines substituted at the 9-position retain receptor affinity but lose selectivity for the **adenosine** A2a and A3 receptors over other **adenosine** receptors. Replacement of the furan moiety present in the pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine with a Ph or a substituted aromatic ring abolishes affinity at all the **adenosine** receptor subtypes, demonstrating that the furanyl ring is a necessary structural element to guarantee interaction with the **adenosine** receptor surface; replacement of the furan ring with an ortho-ethoxy-substituted aromatic ring did not enhance affinity. Introduction of a N-methylpiperazinomethyl or morpholinomethyl function at the 5' position of the furanyl ring of I or introduction of a methylsulfanyl moiety at the 9-position of pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines yields inhibitors with improved water solubilities but reduced affinities for **adenosine** A2a and A3 receptors.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:67295 CAPLUS
DOCUMENT NUMBER: 138:247936
TITLE: Synthesis and Biological Effects of Novel 2-Amino-3-naphthoylthiophenes as Allosteric Enhancers of the A1 **Adenosine** Receptor
AUTHOR(S): **Baraldi, Pier Giovanni**; Romagnoli, Romeo; Pavani, Maria Giovanna; Nunez, Maria del Carmen; Tabrizi, Mojgan Aghazadeh; Shryock, John C.; **Leung, Edward**; Moorman, Allan R.; Uluoglu, Canan; Iannotta, Valeria; Merighi, Stefania; **Borea, Pier Andrea**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy
SOURCE: Journal of Medicinal Chemistry (2003), 46(5), 794-809
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:247936

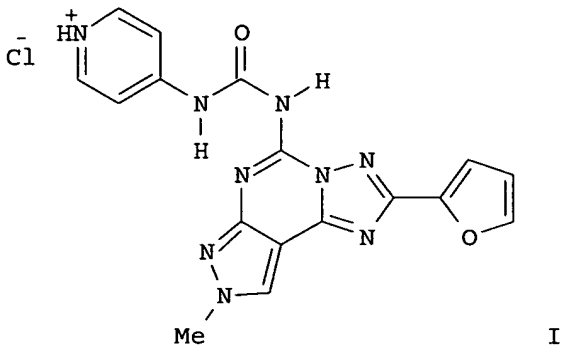
AB The current study describes the synthesis and biol. evaluation of a novel series of 2-amino-3-naphthoylthiophenes, with variable modifications at the 4- and 5-position of the thiophene as well as the naphthoyl ring. Allosteric enhancer activity was measured in several ways: (1) evaluating the effect on forskolin-stimulated cAMP accumulation in the presence of an A1-**adenosine** agonist (CPA) in Chinese hamster ovary (CHO) cells expressing the cloned human A1-**adenosine** receptor (hA1AR); (2) ability of these compds. to displace the binding of [3H]DPCPX, [3H]ZM 241385, and [3H]MRE 3008F20 to the ligand binding site of CHO cells expressing the hA1, hA2A, and hA3 **adenosine** receptors, resp.; (3) effect on the binding of [3H]CCPA to membranes from CHO cells expressing hA1AR, to rat brain and human cortex membrane prepns. containing native **adenosine** A1 receptors; (4) kinetics of the dissociation of [3H]CCPA from CHO-hA1 membranes. The pharmacol. assays compared the various activities to that of the reference compound PD 81,723. Several compds. appeared to be better than PD 81,723 to enhance the effect of CPA (and thus reduce cAMP content) in the CHO:hA1 assay. The effect of these compds. at a concentration of 10 μM was slightly greater than that of the same concentration of the PD 81,723 and substantially greater than that of PD 81,723 when responses to 1 μM of each compound were compared. Cycloalkylthiophenes tended to be more potent then their 4,5-di-Me analogs, and in the series of cycloalkylthiophenes, tetrahydrobenzo[b]thiophene derivs. appeared to be more potent than the dihydrocyclopentadien[b]thiophene counterparts. Some of the most potent compds. were tested at a concentration of 10 μM for their affinity as competitors to the antagonist binding site of CHO cells expressing hA1, hA2A, and hA3 **adenosine** receptors. None inhibited binding at the hA2AAR, but most of them inhibited binding to the hA1AR to varying extents (0-19%) as well as to the hA3AR to a substantial degree (0-57%). A good correlation was found between the increments [3H]CCPA binding to A1 receptors expressed in different systems. Unlike the effect on agonist binding, the tested compds. did not increase the binding of the antagonist [3H]DPCPX on hCHO-A1 membranes. No clear-cut structure-activity relation can be observed based on data from the functional assay, but we have identified several compds. which appeared to be more potent than PD 81,723 and that may be selected for further development.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:882885 CAPLUS
DOCUMENT NUMBER: 138:284589
TITLE: **Adenosine** receptors as mediators of both cell proliferation and cell death of cultured human melanoma cells
AUTHOR(S): Merighi, Stefania; Mirandola, Prisco; Milani, Daniela; Varani, Katia; Gessi, Stefania; Klotz, Karl-Norbert; **Leung, Edward; Baraldi, Pier Giovanni ; Borea, Pier Andrea**
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Italy
SOURCE: Journal of Investigative Dermatology (2002), 119(4), 923-933
CODEN: JIDEAE; ISSN: 0022-202X
PUBLISHER: Blackwell Publishing, Inc.

DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Adenosine** displays contradictory effects on cell **growth** : it improves cell proliferation, but it may also induce apoptosis and impair cell survival. Following the pharmacol. characterization of **adenosine** receptor expression on the human melanoma cell line A375, we chose A375 as our cellular model to define how the extracellular **adenosine** signals are conveyed from each receptor. By using selective **adenosine** receptor agonists or antagonists, we found that A2A stimulation reduced cell viability and cell clone formation, whereas, at the same time, it improved cell proliferation. In support of this finding we demonstrated that the stimulation of A2A **adenosine** receptors stably expressed in Chinese hamster ovary cell clone reproduced deleterious effects observed in human melanoma cells. A3 stimulation counteracted A2A-induced cell death but also reduced cell proliferation. Furthermore, we found that A3 stimulation ensures cell survival. We demonstrated that **adenosine** triggers a survival signal via A3 receptor activation and it kills the cell through A2A receptor inducing a signaling pathway that involves protein kinase C and mitogen-activated protein kinases.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:532124 CAPLUS
DOCUMENT NUMBER: 137:232616
TITLE: Synthesis, Biological Properties, and Molecular Modeling Investigation of the First Potent, Selective, and Water-Soluble Human **A3 Adenosine** Receptor **Antagonist**
AUTHOR(S): Maconi, Anna; Pastorin, Giorgia; Da Ros, Tatiana; Spalluto, Giampiero; Gao, Zhan-guo; Jacobson, Kenneth A.; **Baraldi, Pier Giovanni**; Cacciari, Barbara; Varani, Katia; Moro, Stefano; **Borea, Pier Andrea**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Trieste, Trieste, I-34127, Italy
SOURCE: Journal of Medicinal Chemistry (2002), 45(17), 3579-3582
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:232616
GI



I

AB A new, highly potent, selective, and water-soluble antagonist of the hA3 **adenosine** receptor was synthesized and tested in binding and functional assays. Pyridyl substituted pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine hydrochloride I displayed high water solubility (15 mM) and the highest affinity (Ki = 0.01 nM) and selectivity for the hA3 vs. A1, A2A, and A2B receptors (>10000-fold) ever reported. A Schild anal. of the antagonism by I of agonist-induced inhibition of cAMP production in CHO cells expressing the hA3 receptor indicated a KB value of 0.20 nM.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

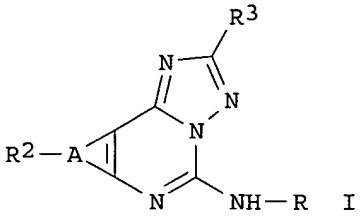
ACCESSION NUMBER: 2002:461311 CAPLUS
DOCUMENT NUMBER: 137:33313
TITLE: Preparation of pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidines and analogs as **adenosine** A3 receptor modulators for therapeutic and diagnostic use
INVENTOR(S): **Baraldi, Pier Giovanni**; **Borea, Pier Andrea**
PATENT ASSIGNEE(S): Medco Research, Inc., USA
SOURCE: U.S., 30 pp., Cont.-in-part of U.S. Ser. No. 154,435.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6407236	B1	20020618	US 1999-379300	19990823
US 6448253	B1	20020910	US 1998-154435	19980916
CA 2332007	AA	20000323	CA 1999-2332007	19990915
WO 2000015231	A1	20000323	WO 1999-US21103	19990915
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9962482	A1	20000403	AU 1999-62482	19990915
AU 749211	B2	20020620		
GB 2353527	A1	20010228	GB 2000-27879	19990915

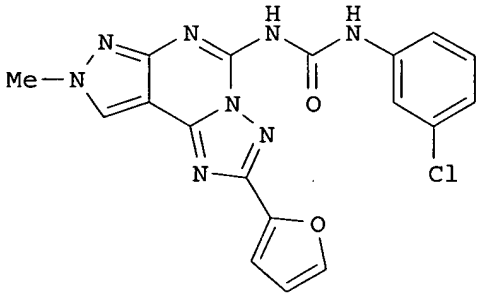
GB 2353527	B2	20040225			
BR 9913766	A	20010605	BR 1999-13766		19990915
TR 200003461	T2	20010621	TR 2000-200003461		19990915
DE 19983530	T	20011108	DE 1999-19983530		19990915
CH 692132	A	20020228	CH 1999-1201		19990915
JP 2002524519	T2	20020806	JP 2000-569815		19990915
NZ 509149	A	20030829	NZ 1999-509149		19990915
ES 2204262	A1	20040416	ES 2001-50007		19990915
ES 2204262	B1	20050301			
SE 2000003984	A	20001222	SE 2000-3984		20001101
SE 522578	C2	20040217			
NO 2000005508	A	20010315	NO 2000-5508		20001101
NO 318078	B1	20050131			
LU 90687	A1	20001219	LU 2000-90687		20001206
ZA 2001001626	A	20011213	ZA 2001-1626		20010227
HK 1035671	A1	20050218	HK 2001-106364		20010907
US 2003144266	A1	20030731	US 2002-134219		20020426
US 6921825	B2	20050726			
US 2006040959	A1	20060223	US 2005-169311		20050627
PRIORITY APPLN. INFO.:			US 1998-154435	A2	19980916
			US 1999-379300	A	19990823
			WO 1999-US21103	W	19990915
			US 2002-134219	A3	20020426

OTHER SOURCE(S): MARPAT 137:33313

GI



I



II

AB Title compds. I [wherein A = imidazole, pyrazole, or triazole; R = CXR1, CXN(R1)2, CXOR1, CXSR1, SOnR1, SOnSR1, or SOnN(R1)2; R1 = H, (hetero)aryl, heterocyclyl, alkanoyl, or (un)substituted alkyl, alkenyl, or alkynyl; or N(R1)2 = azetidinyl or 5-6 membered heterocyclyl; R2 = H or (un)substituted alkyl, alkenyl, aralkyl, or (hetero)aryl; R3 = (un)substituted (benzo)furanyl, (benzo)pyrrolyl, or (benzo)thiophenyl; X = O, S, or NR1; n = 0-2; or pharmaceutically acceptable salts thereof] were prepared as selective A3 **adenosine** receptor agonists. Thus, 3-amino-1H-pyrazole-4-carbonitrile was methylated, treated with tri-Et orthoformate to give the imidate, and cyclized with 2-furoic acid hydrazide to give 8-methyl-2-(2-furyl)pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine (45%). Amination (53%) and addition of 3-chlorophenyl isocyanate (98%) afforded II, which exhibited binding affinity at the A1, A2, and A3 receptors with Ki values of 5,045 nM, >10,1000 nM, and 0.22 nM, resp. I are useful for the treatment disorders caused by excessive activation of the A3 receptor, such as hypertension, inflammation, mast

cell degranulation, cardiac hypoxia, allergic disease, and for protection against cerebral ischemia (no data). In addition, I are useful in diagnostic applications to determine the relative binding of other compds. to the A3 receptor. For instance, the compds. can be labeled, for example with fluorescent or radiolabels, and the labels used in vivo or in vitro to determine the presence of **tumor** cells which possess a high concentration of **adenosine** A3 receptors.

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 34 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:119023 CAPLUS
DOCUMENT NUMBER: 136:380449
TITLE: Binding thermodynamics at the human A3 **adenosine** receptor
AUTHOR(S): Merighi, Stefania; Varani, Katia; Gessi, Stefania; Klotz, Karl-Norbert; **Leung, Edward**; **Baraldi, Pier Giovanni**; **Borea, Pier Andrea**
CORPORATE SOURCE: Pharmacology Unit, Department of Clinical and Experimental Medicine, Centro Nazionale di Eccellenza per lo Sviluppo di Metodologie Innovative per lo Studio ed il Trattamento delle Patologie Infiammatorie, University of Ferrara, Ferrara, 44100, Italy
SOURCE: Biochemical Pharmacology (2002), 63(2), 157-161
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The thermodn. parameters ΔG°, ΔH° and ΔS° of the binding equilibrium of six **adenosine** receptor agonists and five **antagonists** at **adenosine A3** receptors were determined by means of affinity measurements at six different temps. (4, 10, 15, 20, 25 and 30°) and van't Hoff plots were constructed. Affinity consts. were measured on Chinese hamster ovary (CHO) cells transfected with the human A3 receptors by inhibition assays of the binding of the selective A3 antagonist [3H]MRE 3008F20. The van't Hoff plots were linear for agonists and antagonists in the temperature range 4-30°. Their thermodn. parameters fall in the ranges $21 \leq \Delta H° \leq 67$ kJ mol-1 and $208 \leq \Delta S° \leq 410$ J (K mol)-1 for agonists and $-52 \leq \Delta H° \leq -9$ kJ mol-1 and $16 \leq \Delta S° \leq 81$ J (K/mol)-1 for antagonists, showing that agonist binding is always totally entropy-driven while antagonist binding is enthalpy- and entropy-driven. The results are discussed with the aim of obtaining new details on the nature of the forces driving the A3 binding at a mol. level.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:86749 CAPLUS
DOCUMENT NUMBER: 136:257615
TITLE: A3 **adenosine** receptors in human neutrophils and promyelocytic HL60 cells: a pharmacological and biochemical study
AUTHOR(S): Gessi, Stefania; Varani, Katia; Merighi, Stefania; Cattabriga, Elena; Iannotta, Valeria; **Leung,**

Edward; Baraldi, Pier Giovanni;
Borea, Pier Andrea
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Ferrara, Italy
SOURCE: Molecular Pharmacology (2002), 61(2), 415-424
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This work compares the pharmacol. and biochem. properties of A3 **adenosine** receptors in human polymorphonuclear neutrophil granulocytes (PMNs) and promyelocytic HL60 cells. The gene expression of A3 receptors was examined by reverse transcription-polymerase chain reaction expts., whereas the amount of A3 subtype on the plasma membrane was quantified by using the high-affinity and selective A3 antagonist [3H]MRE 3008F20. Saturation expts. reveal a single high-affinity binding site with KD values of 2.3, 2.6 nM, and Bmax values of 430, 345 31 fmol/mg of protein for PMNs and HL60 cells, resp. Competition of radioligand binding by **adenosine** ligands displays a rank order of potency typical of the A3 subtype. EC50 values of N6-(3-iodo-benzyl)-2-chloro-**adenosine** -5'-N-methyluronamide (CI-IB-MECA) for inhibition of cAMP levels via A3 receptors are in good agreement with the binding data; furthermore, the response is potently inhibited by MRE 3008F20. In contrast, the high micromolar concns. of CI-IB-MECA and MRE 3008F20 in stimulating and blocking Ca2+ mobilization, resp., are not completely consistent with the involvement of an A3 receptor. Furthermore, an important finding of this work is that the inhibition of PMNs oxidative burst is predominantly A2A-mediated, even though an effect of A3 subtype could not be excluded. This conclusion is based on potent blockade of CI-IB-MECA-mediated inhibition of oxidative burst by SCH 58261 and a minor but significant blockade by MRE 3008F20. In conclusion, HL60 cells express A3 receptors similar to those in PMNs, thus providing a useful model for investigation of biochem. pathways leading to A3 receptor activation.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:27221 CAPLUS
DOCUMENT NUMBER: 136:241075
TITLE: Synthesis, Biological Activity, and Molecular Modeling Investigation of New Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine Derivatives as Human **A3 Adenosine** Receptor **Antagonists**
AUTHOR(S): **Baraldi, Pier Giovanni**; Cacciari, Barbara; Moro, Stefano; Spalluto, Giampiero; Pastorin, Giorgia; Da Ros, Tatiana; Klotz, Karl-Norbert; Varani, Katia; Gessi, Stefania; **Borea, Pier Andrea**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche and Dipartimento di Medicina Clinica e Sperimentale-Sezione di Farmacologia, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Journal of Medicinal Chemistry (2002), 45(4), 770-780
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:241075

AB A new series of pyrazolotriazolopyrimidines bearing different substitutions on the phenylcarbamoyl moieties at the N5 position, being highly potent and selective human **A3 adenosine** receptor **antagonists**, is described. The compds. represent an extension and an improvement of our previous work on this class of compds. (J. Med. Chemical 1999, 42, 4473-4478; J. Med. Chemical 2000, 43, 4768-4780). All the synthesized compds. showed A3 **adenosine** receptor affinity in the subnanomolar range and high levels of selectivity in radioligand binding assays at the human A1, A2A, A2B, and A3 **adenosine** receptors. In particular, the effect of the substitution and its position on the Ph ring have been studied. From binding data, it is evident that the unsubstituted derivs. on the Ph ring (e.g., compound 59, hA3 = 0.16 nM, hA1/hA3 = 3713, hA2A/hA3 = 2381, hA2B/hA3 = 1388) showed the best profile in terms of affinity and selectivity at the human A3 **adenosine** receptors. The introduction of a sulfonic acid moiety at the para position on the Ph ring was attempted in order to design water soluble derivs. However, this substitution led to a dramatic decrease of affinity at all four **adenosine** receptor subtypes. A computer-generated model of the human A3 receptor was built and analyzed to better interpret these results, demonstrating that steric control, in particular at the para position on the Ph ring, plays a fundamental role in the receptor interaction. Some of the synthesized compds. proved to be full antagonists in a specific functional model, where the inhibition of cAMP-generation by IB-MECA was measured in membranes of CHO cells stably transfected with the human A3 receptor with IC50 values in the nanomolar range, with a statistically significative linear relationship with the binding data.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 37 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:879918 CAPLUS

DOCUMENT NUMBER: 136:161304

TITLE: Pharmacological and biochemical characterization of **adenosine** receptors in the human malignant melanoma A375 cell line

AUTHOR(S): Merighi, Stefania; Varani, Katia; Gessi, Stefania; Cattabriga, Elena; Iannotta, Valeria; Ulouglu, Canan; **Leung, Edward**; **Borea, Pier Andrea**

CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, Centro Nazionale Di Eccellenza Per Lo Sviluppo Di Metodologie Innovative Per Lo Studio Ed II Trattamento Delle Patologie Infiammatorie, University of Ferrara, Italy

SOURCE: British Journal of Pharmacology (2001), 134(6), 1215-1226
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 1 The present work characterizes, from a pharmacol. and biochem. point of view, **adenosine** receptors in the human malignant melanoma A375 cell line. 2 **Adenosine** receptors were detected by RT-PCR expts. A1 receptors were characterized using [3H]-DPCPX binding with a KD of 1.9±0.2 nM and Bmax of 23±7 fmol mg-1 of protein. A2A receptors were studied with [3H]-SCH 58261 binding and revealed a KD of 5.1±0.2 nM and a Bmax of 220±7 fmol mg-1 of protein. A3 receptors were studied with the new **A3 adenosine** receptor **antagonist**

[3H]-MRE 3008F20, the only A3 selective radioligand currently available. Saturation expts. revealed a single high affinity binding site with KD of 3.3±0.7 nM and Bmax of 291±50 fmol mg-1 of protein. 3 The pharmacol. profile of radioligand binding on A375 cells was established using typical **adenosine** ligands which displayed a rank order of potency typical of the different **adenosine** receptor subtype. 4 Thermodn. data indicated that radioligand binding to **adenosine** receptor subtypes in A375 cells was entropy- and enthalpy-driven. 5 In functional assays the high affinity A2A agonists HE-NECA, CGS 21680 and A2A-A2B agonist NECA were able to increase cAMP accumulation in A375 cells whereas A3 agonists Cl-IB-MECA, IB-MECA and NECA were able to stimulate Ca2+ mobilization. 6 In conclusion, all these data indicate, for the first time, that **adenosine** receptors with a pharmacol. and biochem. profile typical of the A1, A2A, A2B and A3 receptor subtype are present on A375 melanoma cell line.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

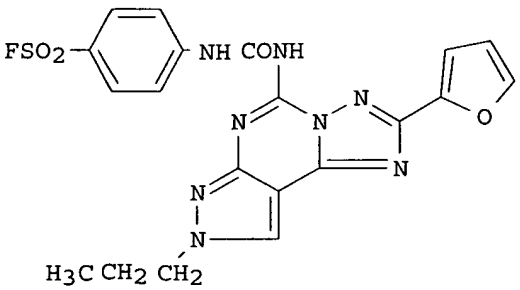
L32 ANSWER 38 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:688899 CAPLUS
DOCUMENT NUMBER: 135:339722
TITLE: Pharmacological and biochemical characterization of A3 **adenosine** receptors in Jurkat T cells
AUTHOR(S): Gessi, Stefania; Varani, Katia; Merighi, Stefania; Morelli, Anna; Ferrari, Davide; **Leung, Edward**; **Baraldi, Pier Giovanni**; Spalluto, Giampiero; **Borea, Pier Andrea**
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Ferrara, 44100, Italy
SOURCE: British Journal of Pharmacology (2001), 134(1), 116-126
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present work was devoted to the study of A3 **adenosine** receptors in Jurkat cells, a human leukemia line. The A3 subtype was found by RT-PCR expts. and characterized by using the new **A3 adenosine** receptor **antagonist** [3H]-MRE 3008F20, the only A3 selective radioligand currently available. Saturation expts. revealed a single high affinity binding site with KD of 1.9 nM and Bmax of 1.3 pmol mg-1 of protein. The pharmacol. profile of [3H]-MRE 3008F20 binding on Jurkat cells was established using typical **adenosine** ligands which displayed a rank order of potency typical of the A3 subtype. Thermodn. data indicated that [3H]-MRE 3008F20 binding to A3 subtype in Jurkat cells was entropy- and enthalpy-driven, according with that found in cells expressing the recombinant human A3 subtype. In functional assays the high affinity A3 agonists Cl-IB-MECA and IB-MECA were able to inhibit cAMP accumulation and stimulate Ca2+ release from intracellular Ca2+ pools followed by Ca2+ influx. The presence of the other **adenosine** subtypes was investigated in Jurkat cells. A1 receptors were characterized using [3H]-DPCPX binding with a KD of 0.9 nM and Bmax of 42 fmol mg-1 of protein. A2A receptors were studied with [3H]-SCH 58261 binding and revealed a KD of 2.5 nM and a Bmax of 1.4 pmol mg-1 of protein. In conclusion, by the first antagonist radioligand [3H]-MRE 3008F20 the authors could demonstrate the existence of functional A3 receptors on Jurkat cells.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:514232 CAPLUS
DOCUMENT NUMBER: 135:251425
TITLE: Fluorosulfonyl- and bis-(β-chloroethyl)amino-phenylamino functionalized pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine derivatives: irreversible antagonists at the human A3 **adenosine** receptor and molecular modeling studies
AUTHOR(S): **Baraldi, Pier Giovanni**; Cacciari, Barbara; Moro, Stefano; Romagnoli, Romeo; Ji, Xiao-duo; Jacobson, Kenneth A.; Gessi, Stefania; **Borea, Pier Andrea**; Spalluto, Giampiero
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Journal of Medicinal Chemistry (2001), 44(17), 2735-2742
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A series of pyrazolotriazolopyrimidines was previously reported to be highly potent and selective human **A3 adenosine** receptor **antagonists** (Baraldi et al. J. Med. Chemical 2000, 43, 4768-4780). A derivative having a Me group at the N8 pyrazole combined with a 4-methoxyphenylcarbamoyl moiety at N5 position, displayed a Ki value at the hA3 receptor of 0.2 nM. We now describe chemical reactive derivs. which act as irreversible inhibitors of this receptor. Electrophilic groups, specifically sulfonyl fluoride and nitrogen mustard (bis-(β-chloroethyl)amino) moieties, have been incorporated at the 4-position of the aryl urea group. Membranes containing the recombinant hA3 receptor were preincubated with the compds. and washed exhaustively. The loss of ability to bind radioligand following this treatment indicated irreversible binding. The most potent compound in irreversibly binding to the receptor was I, which contained a sulfonyl fluoride moiety and a Pr group at the N8 pyrazole nitrogen. The bis-(β-chloroethyl)amino derivs. displayed a much smaller degree of irreversible binding than the sulfonyl fluoride derivs. A computer-generated model of the human A3 receptor was built and analyzed to help interpret these results. The model of the A3 transmembrane region was derived using primary sequence

comparison, secondary structure predictions, and three-dimensional homol. building, using the recently published crystal structure of rhodopsin as a template. According to our model, sulfonyl fluoride derivs. could dock within the hypothetical TM binding domain, adopting two different energetically favorable conformations. We have identified two amino acids, Ser247 and Cys251, both in TM6, as potential nucleophilic partners of the irreversible binding to the receptor.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:342062 CAPLUS
DOCUMENT NUMBER: 135:146779
TITLE: Pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine derivatives: a new pharmacological tool for the characterization of the human A3 **adenosine** receptor
AUTHOR(S): **Baraldi, Pier Giovanni**; Cacciari, Barbara; Romagnoli, Romeo; Spalluto, Giampiero; Varani, Katia; Gessi, Stefania; Merighi, Stefania; **Borea, Pier Andrea**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Drug Development Research (2001), 52(1/2), 406-415
CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Adenosine** regulates many physiol. functions by interaction with four different G-protein-coupled receptors classified as A1, A2A, A2B, and A3. While **adenosine** A1 and A2A receptor subtypes have been pharmacol. characterized through the use of selective ligands, the A2B and A3 **adenosine** receptor subtypes are presently under study to better understand their physio-pathol. functions. In particular, activation of **adenosine** A3 receptors has been shown to stimulate phospholipase C and D and to inhibit adenylate cyclase. Activation of A3 **adenosine** receptors also causes the release of inflammatory mediators such as histamine from mast cells, which are responsible for processes such as inflammation and hypotension. For these reasons, it has been suggested that **A3 adenosine** receptor **antagonists** can be considered potential drugs for the treatment of asthma and inflammation. In the last few years different classes of heterocyclic compds. have been identified as **A3 adenosine antagonists**, but none of the tested compds. showed significant selectivity for A3 **adenosine** receptor subtype. Herein, we report our recent results on a class of pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine derivs. as a new class of potent and selective human **A3 adenosine** receptor **antagonists**. The full characterization of the first high-affinity radioligand antagonist for this receptor subtype, designated [3H] MRE3008F20, is briefly summarized.
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 41 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:891037 CAPLUS
DOCUMENT NUMBER: 134:247274
TITLE: New potent and selective human **adenosine** **A3** receptor **antagonists**

AUTHOR(S): **Baraldi, P. G.; Borea, P. A.**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Trends in Pharmacological Sciences (2000), 21(12), 456-459
CODEN: TPHSDY; ISSN: 0165-6147
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 25 refs., describing evaluation of pathophysiol. role of human **adenosine** A3 receptors by subtype-selective agonists and antagonists, design of selective A3 receptor ligands (mainly antagonists), and preparation of a selective high-affinity radiolabeled compound ([3H]MRE 3008F20).
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 42 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:818494 CAPLUS
DOCUMENT NUMBER: 134:131485
TITLE: Pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine Derivatives as Highly Potent and Selective Human **A3 Adenosine** Receptor **Antagonists**: Influence of the Chain at the N8 Pyrazole Nitrogen
AUTHOR(S): **Baraldi, Pier Giovanni**; Cacciari, Barbara; Romagnoli, Romeo; Spalluto, Giampiero; Moro, Stefano; Klotz, Karl-Norbert; **Leung, Edward**; Varani, Katia; Gessi, Stefania; Merighi, Stefania; **Borea, Pier Andrea**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche and Dipartimento di Medicina Clinica e Sperimentale-Sezione di Farmacologia, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Journal of Medicinal Chemistry (2000), 43(25), 4768-4780
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An enlarged series of pyrazolotriazolopyrimidines previously reported, in preliminary form (Baraldi et al. J. Med. Chemical 1999, 42, 4473-4478), as highly potent and selective human **A3 adenosine** receptor **antagonists** is described. The synthesized compds. showed A3 **adenosine** receptor affinity in the sub-nanomolar range and high levels of selectivity evaluated in radioligand binding assays at human A1, A2A, A2B, and A3 **adenosine** receptors. In particular, the effect of the chain at the N8 pyrazole nitrogen was analyzed. This study allowed us to identify the derivative with the Me group at the N8 pyrazole combined with the 4-methoxyphenylcarbamoyl moiety at the N5 position as the compound with the best binding profile in terms of both affinity and selectivity (hA3 = 0.2 nM, hA1/hA3 = 5485, hA2A/hA3 = 6950, hA2B/hA3 = 1305). All the compds. proved to be full antagonists in a specific functional model where the inhibition of cAMP generation by IB-MECA was measured in membranes of CHO cells stably transfected with the human A3 receptor. The new compds. are among the most potent and selective A3 antagonists so far described. The derivs. with higher affinity at human A3 **adenosine** receptors proved to be antagonists, in the cAMP assay, capable of inhibiting the effect of

IB-MECA with IC50 values in the nanomolar range, with a trend strictly similar to that observed in the binding assay. Also a mol. modeling study was carried out, with the aim to identify possible pharmacophore maps. In fact, a sterically controlled structure-activity relationship was found for the N8 pyrazole substituted derivs., showing a correlation between the calculated mol. volume of pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine derivs.
and their exptl. Ki values.
REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 43 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:458360 CAPLUS
TITLE: Synthesis and preliminary biological evaluation of [3H]-MRE 3008-F20: the first high affinity radioligand antagonist for the human A3 **adenosine** receptors
AUTHOR(S): **Baraldi, Pier Giovanni**; Cacciari, Barbara; Romagnoli, Romeo; Varani, Katia; Merighi, Stefania; Gessi, Stefania; **Borea, Pier Andrea**; **Leung, Edward**; Hickey, Sarah L.; Spalluto, Giampiero
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(12), 1403
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; Errata
LANGUAGE: English
AB Unavailable

L32 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:203123 CAPLUS
DOCUMENT NUMBER: 132:303548
TITLE: A3 **adenosine** receptor ligands: history and perspectives
AUTHOR(S): **Baraldi, Pier Giovanni**; Cacciari, Barbara; Romagnoli, Romeo; Merighi, Stefania; Varani, Katia; **Borea, Pier Andrea**; Spalluto, Giampiero
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, I-44100, Italy
SOURCE: Medicinal Research Reviews (2000), 20(2), 103-128
CODEN: MRREDD; ISSN: 0198-6325
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 92 refs. **Adenosine** regulates many physiol. functions through specific cell membrane receptors. On the basis of pharmacol. studies and mol. cloning, four different **adenosine** receptors have been identified and classified as A1, A2A, A2B, and A3. These **adenosine** receptors are members of the G-protein-coupled receptor family. While **adenosine** A1 and A2A receptor subtypes have been pharmacol. characterized through the use of selective ligands, the A3 **adenosine** receptor subtype is presently under study to better understand its physio-pathol. functions. Activation of **adenosine** A3 receptors has been shown to stimulate phospholipase C and D and to inhibit adenylate cyclase. Activation of A3 **adenosine** receptors also causes the release of inflammatory

mediators such as histamine from mast cells. These mediators are responsible for processes such as inflammation and hypotension. It has also been suggested that the A3 receptor plays an important role in brain ischemia, immunosuppression, and bronchospasm in several animal models. Based on these results, highly selective A3 **adenosine** receptor agonists and/or antagonists have been indicated as potential drugs for the treatment of asthma and inflammation, while highly selective agonists have been shown to possess cardioprotective effects. The updated material related to this field of research has been rationalized and arranged to offer an overview of the topic.

REFERENCE COUNT: 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 45 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:190930 CAPLUS
DOCUMENT NUMBER: 132:217158
TITLE: 1,2,4-Triazolo[1,5-c]pyrimidine **adenosine** A3 receptor modulators, preparation thereof, and therapeutic and diagnostic use
INVENTOR(S): **Baraldi, Pier Giovanni; Borea, Pier Andrea**
PATENT ASSIGNEE(S): Medco Research Inc., USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015231	A1	20000323	WO 1999-US21103	19990915
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6448253	B1	20020910	US 1998-154435	19980916
US 6407236	B1	20020618	US 1999-379300	19990823
CA 2332007	AA	20000323	CA 1999-2332007	19990915
AU 9962482	A1	20000403	AU 1999-62482	19990915
AU 749211	B2	20020620		
GB 2353527	A1	20010228	GB 2000-27879	19990915
GB 2353527	B2	20040225		
BR 9913766	A	20010605	BR 1999-13766	19990915
DE 19983530	T	20011108	DE 1999-19983530	19990915
JP 2002524519	T2	20020806	JP 2000-569815	19990915
NZ 509149	A	20030829	NZ 1999-509149	19990915
RU 2250904	C2	20050427	RU 2000-127721	19990915
SE 2000003984	A	20001222	SE 2000-3984	20001101
SE 522578	C2	20040217		
NO 2000005508	A	20010315	NO 2000-5508	20001101
NO 318078	B1	20050131		
LU 90687	A1	20001219	LU 2000-90687	20001206
HK 1035671	A1	20050218	HK 2001-106364	20010907
PRIORITY APPLN. INFO.:			US 1998-154435 A	19980916

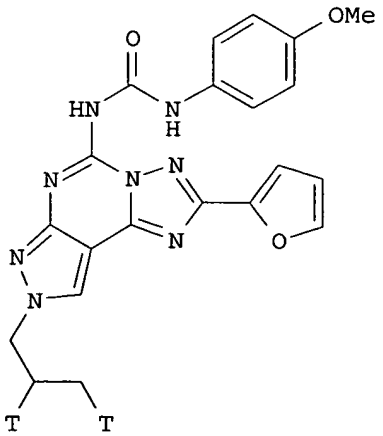
US 1999-379300 A 19990823
WO 1999-US21103 W 19990915

OTHER SOURCE(S): MARPAT 132:217158

AB The title compds. (Markush included), which have selective A3 **adenosine** receptor agonist activity, are provided. These compds. can be used in a pharmaceutical composition to treat disorders caused by excessive activation of the A3 receptor, or can be used in a diagnostic application to determine the relative binding of other compds. to the A3 receptor. The compds. can be labeled, for example with fluorescent or radiolabels, and the labels used in vivo or in vitro to determine the presence of **tumor** cells which possess a high concentration of **adenosine** A3 receptors.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:146874 CAPLUS
DOCUMENT NUMBER: 132:290670
TITLE: Synthesis and preliminary biological evaluation of [3H]-MRE 3008-F20: the first high affinity radioligand antagonist for the human A3 **adenosine** receptors
AUTHOR(S): **Baraldi, Pier Giovanni**; Cacciari, Barbara; Romagnoli, Romeo; Varani, Katia; Merighi, Stefania; Gessi, Stefania; **Borea, Pier Andrea**; **Leung, Edward**; Hickey, Sarah L.; Spalluto, Giampiero
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(3), 209-211
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

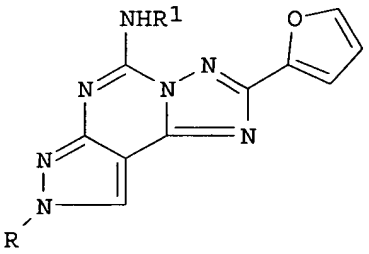
AB The synthesis and the preliminary biol. evaluation of the first high affinity radioligand antagonist for the human A3 **adenosine**

receptor, pyrazolotriazolopyrimidinyl methoxyphenyl urea I ([3H]-MRE 3008-F20) are reported. I bound human A3 receptors expressed in CHO cells with KD and Bmax value of 0.82 ± 0.08 nM and 297 ± 28 fmol/mg of protein, resp. I represents a useful tool for further characterization of A3 **adenosine** receptor subtypes.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 47 OF 47 CAPLUS COPYRIGHT 2006 ACS on STN

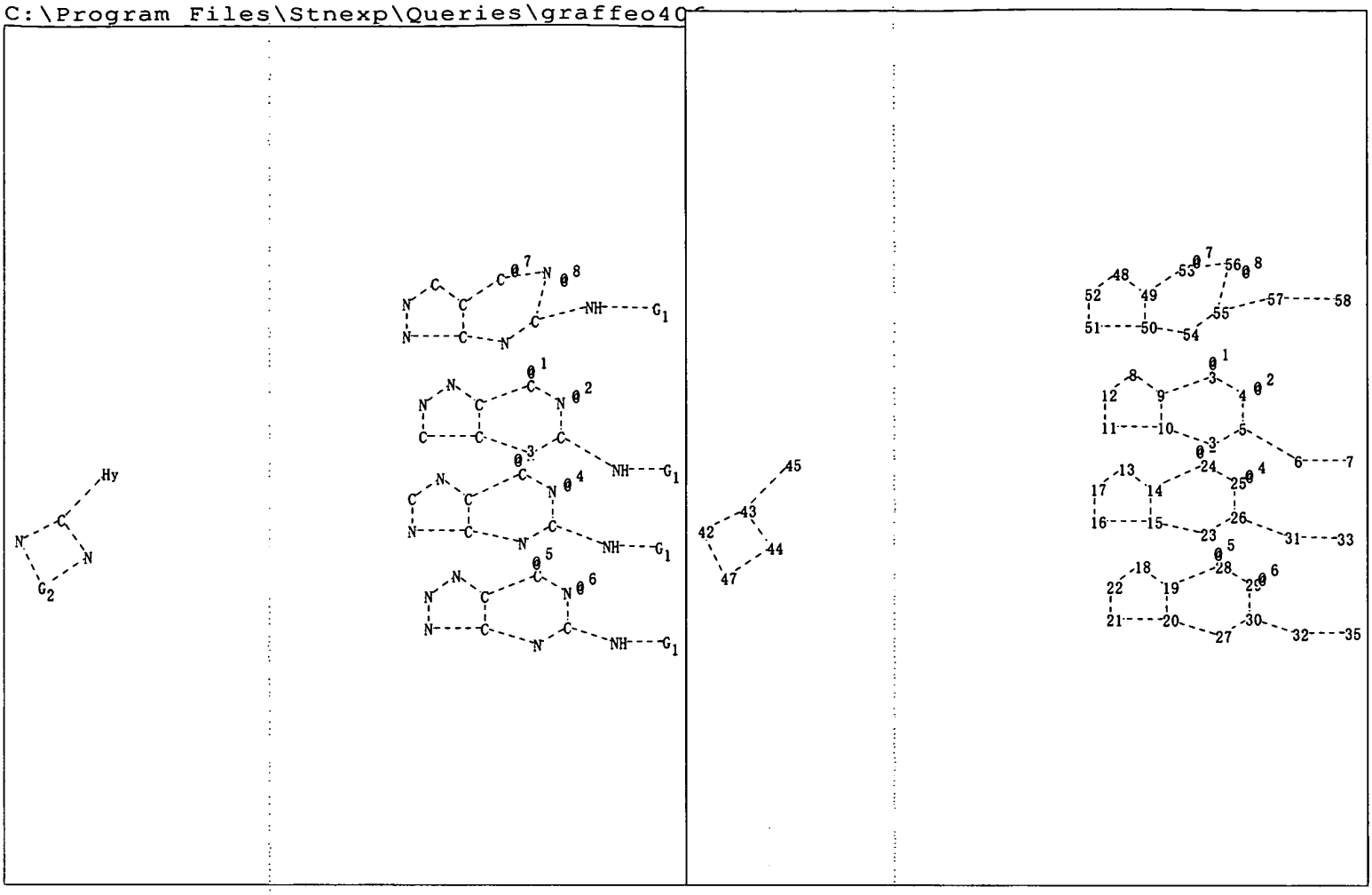
ACCESSION NUMBER: 1999:643387 CAPLUS
DOCUMENT NUMBER: 132:49935
TITLE: Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine derivatives as highly potent and selective human **A3 adenosine** receptor **antagonists**
AUTHOR(S): **Baraldi, Pier Giovanni**; Cacciari, Barbara; Romagnoli, Romeo; Spalluto, Giampiero; Klotz, Karl-Norbert; **Leung, Edward**; Varani, Katia; Gessi, Stefania; Merighi, Stefania; **Borea, Pier Andrea**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche and Dipartimento di Medicina Clinica e Sperimentale-Sezione di Farmacologia, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Journal of Medicinal Chemistry (1999), 42(22), 4473-4478
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The pyrazolotriazolopyrimidines I (R = Ph, Pr, PhCH2CH2, PhCH2CH2CH2; R1 = H, 4-MeOC6H4NHCO, 3-ClC6H4NHCO) were prepared and the structural requirements necessary for recognition by the A3 **adenosine** receptor were studied. A substituted phenylcarbamoyl moiety confers affinity and selectivity for the A3 **adenosine** receptor subtype at the pyrazolotriazolopyrimidine nucleus, while the N5-unsubstituted derivs. lack both affinity and selectivity for human A3 receptors, showing high affinity for A1 and/or A2A receptor subtypes. Substitution at the N8 position with small alkyl groups resulted in higher affinity and selectivity at the human A3 receptor. When N8-Et and N5-4-methoxyphenylcarbamoyl substitutions were combined, the most potent and selective human **A3 adenosine antagonist** I (R

C:\Program Files\Stnexp\Queries\graffeo40



chain nodes :
6 7 31 32 33 35 45 57 58
ring nodes :
2 3 4 5 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
24 25 26 27 28 29 30 42 43 44 47 48 49 50 51 52 53 54 55
56
chain bonds :
5-6 6-7 26-31 30-32 31-33 32-35 43-45 55-57 57-58
ring bonds :
2-5 2-10 3-4 3-9 4-5 8-9 8-12 9-10 10-11 11-12 13-14 13-17
14-15 14-24 15-16 15-23 16-17 18-19 18-22 19-20 19-28 20-21 20-27
21-22 23-26 24-25 25-26 27-30 28-29 29-30 42-43 42-47 43-44 44-47
48-49 48-52 49-50 49-53 50-51 50-54 51-52 53-56 54-55 55-56
exact/norm bonds :
2-5 2-10 3-4 3-9 4-5 5-6 6-7 8-9 8-12 9-10 10-11 11-12 13-14
13-17 14-15 14-24 15-16 15-23 16-17 18-19 18-22 19-20 19-28 20-21
20-27 21-22 23-26 24-25 25-26 26-31 27-30 28-29 29-30 30-32 31-33
32-35 42-43 42-47 43-44 43-45 44-47 48-49 48-52 49-50 49-53 50-51
50-54 51-52 53-56 54-55 55-56 55-57 57-58

G1:C,S

G2:[*1-*2],[*3-*4],[*5-*6],[*7-*8]

Match level :
2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom
19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom
27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS 32:CLASS 33:CLASS 35:CLASS
42:Atom 43:Atom 44:Atom 45:Atom 47:Atom 48:Atom 49:Atom 50:Atom
51:Atom 52:Atom 53:Atom 54:Atom 55:Atom 56:Atom 57:CLASS 58:CLASS

= Et; R1 = 4-MeOC6H4NHCO) was obtained. Thus, the pyrazolotriazolopyrimidine nucleus is a possible template for generating **adenosine** receptor subtype-selective ligands.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d que l6
L3 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L5 186 SEA FILE=REGISTRY SSS FUL L3
L6 34 SEA FILE=CAPLUS ABB=ON PLU=ON L5

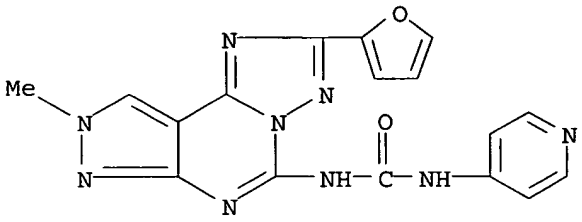
=> d ibib abs hitstr l6 tot

L6 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:204547 CAPLUS
DOCUMENT NUMBER: 144:381790
TITLE: A3 adenosine receptor antagonists delay irreversible synaptic failure caused by oxygen and glucose deprivation in the rat CA1 hippocampus in vitro
AUTHOR(S): Pugliese, Anna Maria; Coppi, Elisabetta; Spalluto, Giampiero; Corradetti, Renato; Pedata, Felicita
CORPORATE SOURCE: Dipartimento di Farmacologia Preclinica e Clinica, Universita' di Firenze, Florence, 50139, Italy
SOURCE: British Journal of Pharmacology (2006), 147(5), 524-532
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of adenosine A3 receptor activation during ischemia-like conditions produced by oxygen and glucose deprivation (OGD) was evaluated with extracellular recordings from the CA1 region of rat hippocampal slices. In all, 7 min of OGD evoked tissue anoxic depolarization (AD, peak at .apprx.7 min from OGD start, n = 20) and were invariably followed by irreversible loss of elec. evoked field epsps (fepsps, n = 42). The selective adenosine A3 antagonists 3-propyl-6-ethyl-5[(ethylthio)carbonyl]-2-phenyl-4-propyl-3-pyridinecarboxylate (MRS 1523, 1-100 nM, n = 31) , N-[9-chloro-2-(2-furanyl)[1,2,4]-triazolo[1,5-c]quinazolin-5-yl]benzeneacetamide (MRS 1220, 100 nM, n = 7) , N-(2-methoxyphenyl)-N'-[2-(3-pyridinyl)-4-quinazolinyl]-urea , (VUF 5574, 100 nM, n = 3) and 5-[[(4-pyridyl)amino]carbonyl]amino-8-methyl-2-(2-furyl)-pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine hydrochloride (1 nM , n = 4) , prevented the irreversible failure of neurotransmission induced by 7 min OGD (n = 45) and the development of AD in 20 out of 22 monitored slices. When tested on OGD episodes of longer duration (8 - 10 min, n = 18), 100 nM MRS 1523 prevented or delayed the appearance of AD and exerted a protective effect on neurotransmission for episodes of up to 9 min duration. In the absence of AD, the fepsp recovery was almost total, regardless of OGD episode duration. These findings support the notion that A3 receptor stimulation is deleterious during ischemia and suggest that selective A3 receptor block may substantially increase the resistance of the CA1 hippocampal region to ischemic damage.
IT **458556-54-2**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A3 adenosine receptor antagonists delay irreversible synaptic failure caused by oxygen and glucose deprivation in rat CA1 hippocampus in vitro)

RN 458556-54-2 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-4-pyridinyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:106016 CAPLUS

DOCUMENT NUMBER: 144:350631

TITLE: Synthesis and Biological Studies of a New Series of 5-Heteroarylcarbamoylaminopyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidines as Human A3 Adenosine Receptor Antagonists. Influence of the Heteroaryl Substituent on Binding Affinity and Molecular Modeling Investigations

AUTHOR(S): Pastorin, Giorgia; Da Ros, Tatiana; Bolcato, Chiara; Montopoli, Christian; Moro, Stefano; Cacciari, Barbara; Baraldi, Pier Giovanni; Varani, Katia; Borea, Pier Andrea; Spalluto, Giampiero

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Trieste, Trieste, I-34127, Italy

SOURCE: Journal of Medicinal Chemistry (2006), 49(5), 1720-1729
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

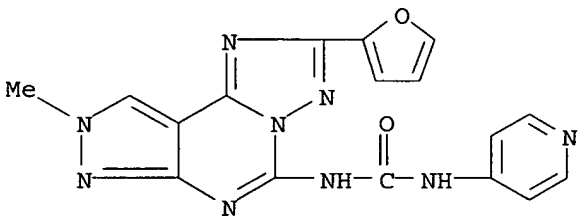
LANGUAGE: English

AB Some pyrazolotriazolopyrimidines bearing different heteroarylcarbamoylamino moieties at the N(5)-position are described. The synthesis of a water soluble compound with high potency and selectivity vs. the human A3 adenosine receptor as antagonist has been reported, and an enlarged series of compds. related to this compound is presented. These compds. showed A3 adenosine receptor affinity in the nanomolar range and different levels of selectivity evaluated in radioligand binding assays at human A1, A2A, A2B, and A3 adenosine receptors. In particular, the effect of the heteroaryl substituents at the N(5) position has been analyzed. This study leads to the recognition that the presence of a pyridinium

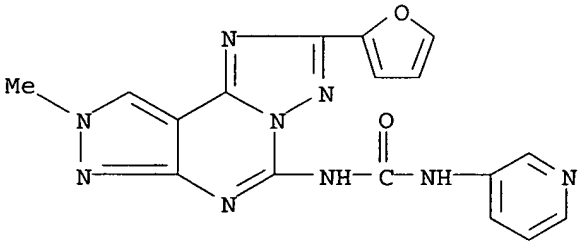
moiety in this position not only increases water solubility but also improves or retains potency and selectivity at the human A3 adenosine receptors. In contrast, replacement of pyridine with different heterocycles produces loss of affinity and selectivity at the human A3 adenosine receptors. A mol. modeling study has been carried out with the aim to explain these various binding profiles.

IT **458556-53-1P 881404-06-4P 881404-08-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 5-heteroarylcarbamoylaminopyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidines as human A3 adenosine receptor antagonists)

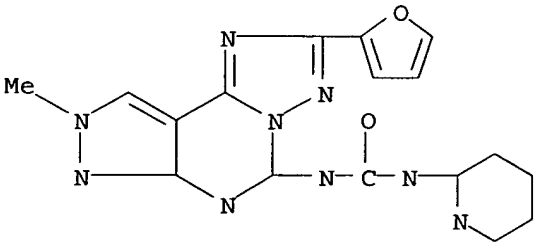
RN 458556-53-1 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 881404-06-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



RN 881404-08-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)

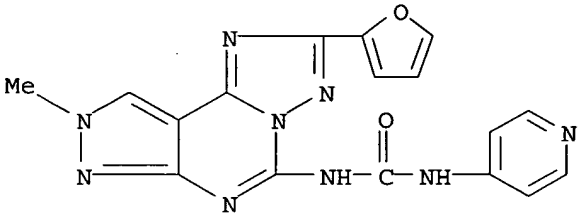


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

IT **458556-54-2P 881404-07-5P 881404-09-7P**
881404-10-0P 881404-11-1P 881404-12-2P
881404-13-3P 881404-14-4P 881404-15-5P
881404-16-6P 881404-17-7P 881404-18-8P
881404-19-9P 881404-20-2P 881404-21-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of 5-heteroarylcarbamoylaminopyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidines as human A3 adenosine receptor antagonists)

RN 458556-54-2 CAPLUS

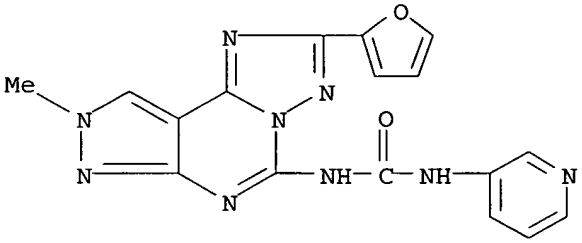
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-4-pyridinyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 881404-07-5 CAPLUS

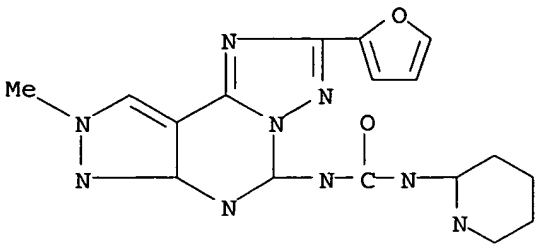
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-3-pyridinyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

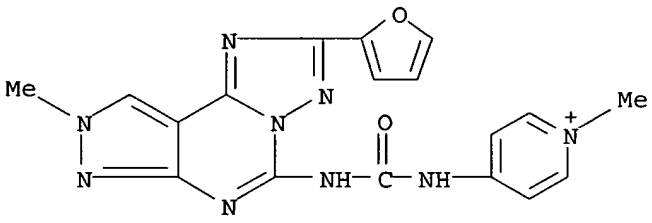
RN 881404-09-7 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-2-pyridinyl-, monohydrochloride (9CI) (CA INDEX NAME)



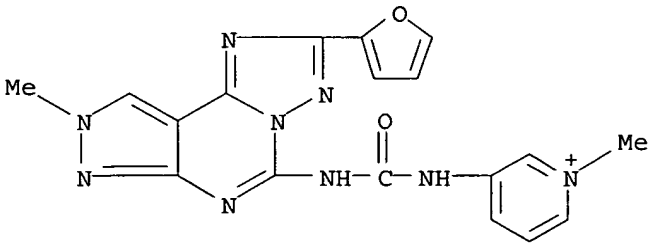
● HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 881404-10-0 CAPLUS
CN Pyridinium, 4-[[[[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-1-methyl-, iodide (9CI) (CA INDEX NAME)



● I^-

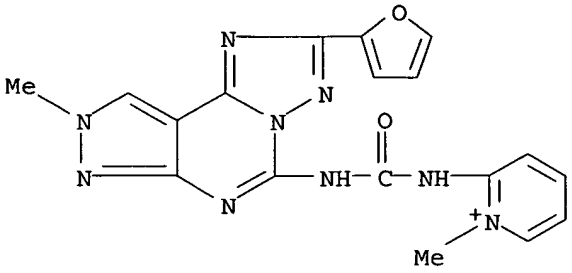
RN 881404-11-1 CAPLUS
CN Pyridinium, 3-[[[[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-1-methyl-, iodide (9CI) (CA INDEX NAME)



● I^-

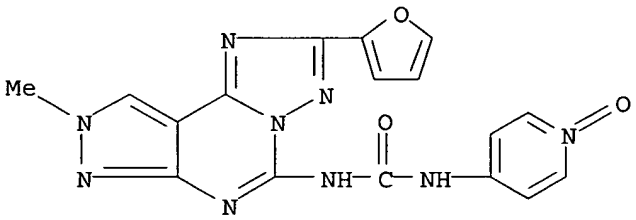
RN 881404-12-2 CAPLUS

CN Pyridinium, 2-[[[[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-1-methyl-, iodide (9CI) (CA INDEX NAME)

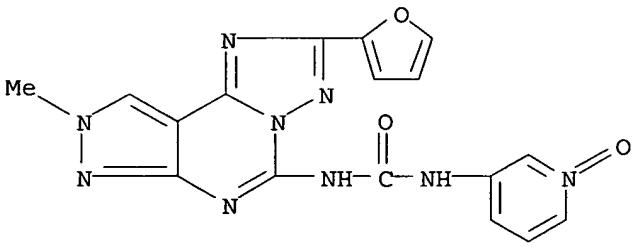


● I^-

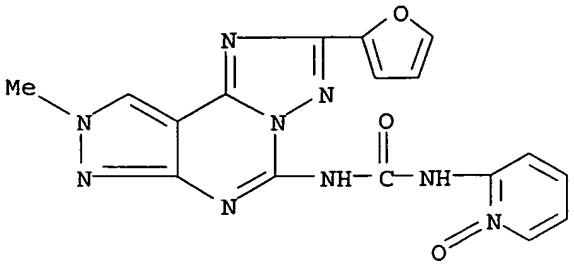
RN 881404-13-3 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-oxido-4-pyridinyl)- (9CI) (CA INDEX NAME)



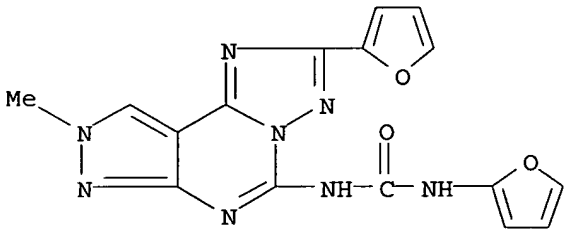
RN 881404-14-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-oxido-3-pyridinyl)- (9CI) (CA INDEX NAME)



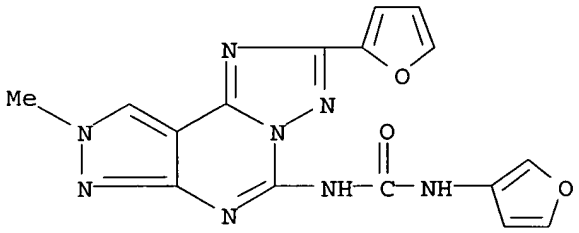
RN 881404-15-5 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-oxido-2-pyridinyl)- (9CI) (CA INDEX NAME)



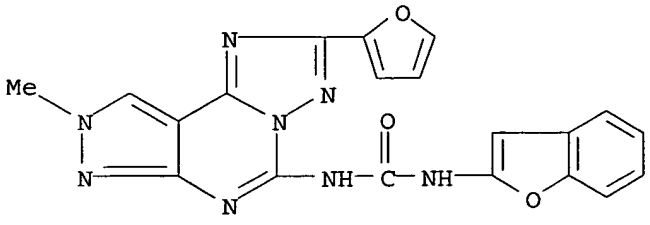
RN 881404-16-6 CAPLUS
CN Urea, N-2-furanyl-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 881404-17-7 CAPLUS
CN Urea, N-3-furanyl-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

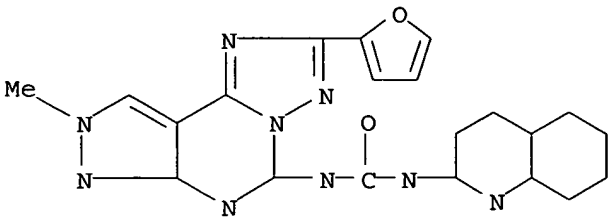


RN 881404-18-8 CAPLUS
CN Urea, N-2-benzofuranyl-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

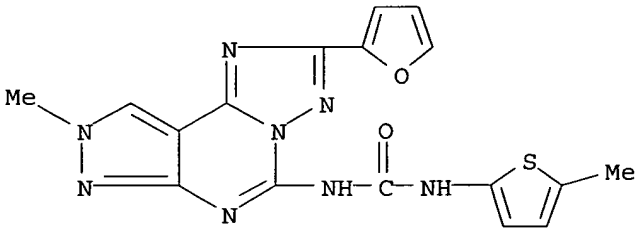


RN 881404-19-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-

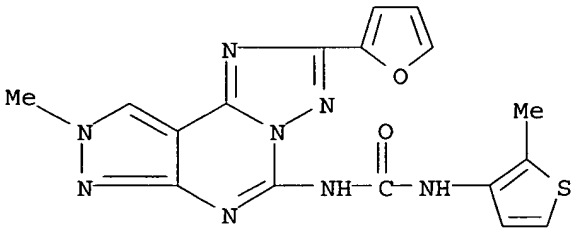
c]pyrimidin-5-yl]-N'-2-quinolinyl- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 881404-20-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(5-methyl-2-thienyl)- (9CI) (CA INDEX NAME)



RN 881404-21-3 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methyl-3-thienyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

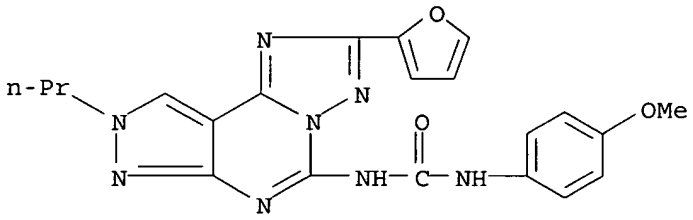
L6 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1346847 CAPLUS
DOCUMENT NUMBER: 144:381438
TITLE: A3 adenosine receptors modulate hypoxia-inducible factor-1α expression in human A375 melanoma cells
AUTHOR(S): Merighi, Stefania; Benini, Annalisa; Mirandola, Prisco; Gessi, Stefania; Varani, Katia; Leung, Edward; MacLennan, Stephen; Baraldi, Pier Giovanni; Borea, Pier Andrea
CORPORATE SOURCE: Department of Clinical and Experimental Medicine-Pharmacology Unit, University of Ferrara,

Ferrara, 44100, Italy
SOURCE: Neoplasia (Ann Arbor, MI, United States) (2005), 7(10), 894-903
CODEN: NEOPFL; ISSN: 1522-8002
PUBLISHER: Neoplasia Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hypoxia-inducible factor-1 (HIF-1) is a key regulator of genes crucial to many aspects of cancer biol. The purine nucleoside, adenosine, accumulates within many tissues under hypoxic conditions, including that of tumors. Because the levels of both HIF-1 and adenosine are elevated within the hypoxic environment of solid tumors, we investigated whether adenosine may regulate HIF-1. Here we show that, under hypoxic conditions (< 2% O2), adenosine upregulates HIF-1α protein expression in a dose-dependent and time-dependent manner, exclusively through the A3 receptor subtype. The response to adenosine was generated at the cell surface because the inhibition of A3 receptor expression, by using small interfering RNA, abolished nucleoside effects. A3 receptor stimulation in hypoxia also increases angiopoietin-2 (Ang-2) protein accumulation through the induction of HIF-1α. In particular, we found that A3 receptor stimulation activates p44/p42 and p38 mitogen-activated protein kinases, which are required for A3-induced increase of HIF-1α and Ang-2. Collectively, these results suggest a cooperation between hypoxic and adenosine signals that ultimately may lead to the increase in HIF-1-mediated effects in cancer cells.

IT **252979-43-4**, MRE 3008F20
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A3 adenosine receptor induced hypoxia-inducible factor-1α protein expression under hypoxic condition in human U87MG glioblastoma cell line)

RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

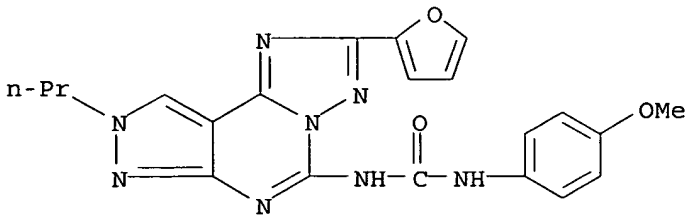
L6 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1162218 CAPLUS
DOCUMENT NUMBER: 144:32441
TITLE: Pharmacological characterization of novel adenosine ligands in recombinant and native human A2B receptors
AUTHOR(S): Varani, Katia; Gessi, Stefania; Merighi, Stefania; Vincenzi, Fabrizio; Cattabriga, Elena; Benini, Annalisa; Klotz, Karl-Norbert; Baraldi, Pier Giovanni; Tabrizi, Mojgan Aghazadeh; MacLennan, Stephen; Leung, Edward; Borea, Pier Andrea

CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Ferrara, 44100, Italy
SOURCE: Biochemical Pharmacology (2005), 70(11), 1601-1612
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study was designed to evaluate the effects of novel and recognized compds. at human recombinant A2B adenosine receptors expressed in Chinese hamster ovary (hA2BCHO), in human embryonic kidney 293 (hA2BHEK-293) and at endogenous A2B receptors in human mast cells (HMC-1). Saturation binding expts. performed using the new high affinity A2B adenosine radioligand [3H]-N-benzo[1,3]dioxol-5-yl-2-[5-(2,6-dioxo-1,3-dipropyl-2,3,6,7-tetra hydro-1H-purin-8-yl)-1-methyl-1H-pyrazol-3-yloxy]-acetamide ([3H]-MRE 2029F20) revealed a single class of binding sites in hA2BCHO, hA2BHEK-293 and HMC-1 cells with K D (nM) of 1.65±0.18, 2.83±0.34, 2.62±0.27 and B max (fmol/mg protein) of 36±4, 475±50 and 128±15, resp. The pharmacol. profile of new compds., determined in inhibition binding expts. in hA2BHEK-293 cells using [3H]-MRE 2029F20, showed a rank order of potency typical of the A2B receptors with K i values in the range 3.2-28 nM. In functional assays, recognized agonists and antagonists were studied by evaluating their capability to modulate the cAMP production in hA2BCHO and in HMC-1 cells. Novel compds. were able to decrease NECA-stimulated cAMP production in hA2BCHO and in HMC-1 cells showing a high potency. New compds. were also able to inhibit cAMP levels in the absence of NECA and in the presence of forskolin stimulation in hA2BCHO and in HMC-1 cells. In HEK-293 cells MRE 2029F20 reduced cAMP basal levels with an IC50 value of 2.9±0.3 nM. These results suggest that novel compds. are antagonists with an inverse agonist activity in recombinant and native human A2B receptors.

IT **252979-43-4**, MRE 3008F20
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. characterization of novel adenosine ligands in recombinant and native human A2B receptors)

RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:703873 CAPLUS
DOCUMENT NUMBER: 143:338940
TITLE: Autocorrelation of Molecular Electrostatic Potential Surface Properties Combined with Partial Least Squares

Analysis as New Strategy for the Prediction of the Activity of Human A3 Adenosine Receptor Antagonists

AUTHOR(S): Moro, Stefano; Bacilieri, Magdalena; Cacciari, Barbara; Spalluto, Giampiero

CORPORATE SOURCE: Molecular Modeling Section, Dipartimento di Scienze Farmaceutiche, Universita di Padova, Padua, I-35131, Italy

SOURCE: Journal of Medicinal Chemistry (2005), 48(18), 5698-5704
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

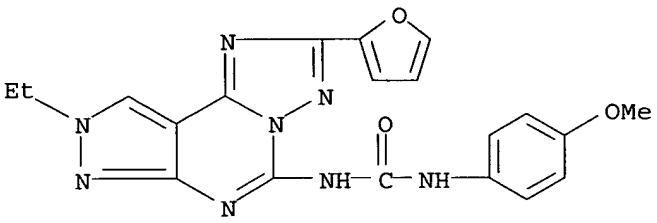
LANGUAGE: English

AB The combination of mol. electrostatic potential (MEP) surface properties (autocorrelation vectors) with the conventional partial least squares (PLS) anal. has been used for the prediction of the human A3 receptor antagonist activities. Three-hundred-fifty-eight structurally diverse human A3 receptor antagonists have been utilized to generate a novel ligand-based three-dimensional structure-activity relation. Remarkably, our chemical library includes all 21 important chemical classes of human A3 antagonists currently discovered, and it represents the largest mol. collection used to generate a general human A3 antagonist structure-activity relation. A robust quant. model has been obtained as described by both cross-validated correlation coefficient (rcv = 0.81) and prediction capability (rpred = 0.82). The proposed MEP/PLS approach can be considered as an alternative hit identification tool in virtual screening applications.

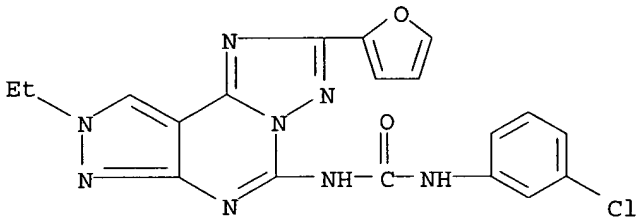
IT **252979-41-2 252979-42-3 252979-43-4**
252979-44-5 252979-45-6 252979-46-7
252979-47-8 252979-48-9 261629-22-5
261629-23-6 261629-24-7 261629-25-8
261629-26-9 261629-27-0 261629-28-1
261629-29-2 264623-54-3 321661-27-2
321661-29-4 321661-35-2 321661-36-3
321661-37-4 321661-38-5 361484-61-9
361484-62-0 361484-63-1 361484-64-2
385441-71-4 385441-72-5 385441-73-6
385441-74-7 385441-75-8 385441-76-9
385441-77-0 385441-78-1 385441-80-5
385441-82-7 396653-58-0 404011-36-5
404011-37-6 404011-39-8 404011-40-1
404011-41-2 404011-43-4 404011-44-5
404011-45-6 404011-46-7 404011-47-8
404011-49-0 404011-50-3 404011-51-4
404011-52-5 404011-54-7 404011-55-8
404011-56-9 404011-57-0 404011-58-1
404011-59-2 404011-60-5 404011-61-6
404011-62-7 404011-63-8 404011-65-0
404011-66-1 404011-67-2 404011-68-3
404011-69-4 404011-70-7 404011-71-8
404011-72-9 404011-73-0 404011-74-1
404011-75-2 404011-76-3 404011-77-4
404011-78-5 404011-79-6 404011-80-9
404011-81-0 404011-82-1 404011-85-4
827629-36-7 827629-39-0 827629-41-4
827629-42-5 827629-43-6 827629-45-8
827629-46-9 827629-47-0 827629-49-2
827629-50-5 865788-07-4 865788-08-5
865788-09-6 865788-10-9

RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(mol. electrostatic potential surface properties combined with partial least squares anal. for prediction of activity of human A3 adenosine receptor antagonists)

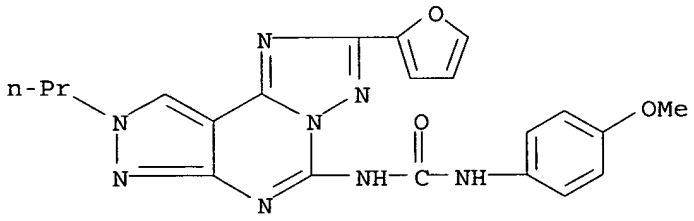
RN 252979-41-2 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



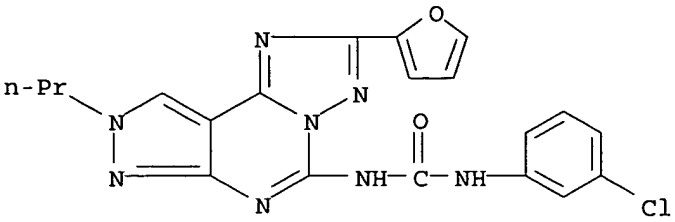
RN 252979-42-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



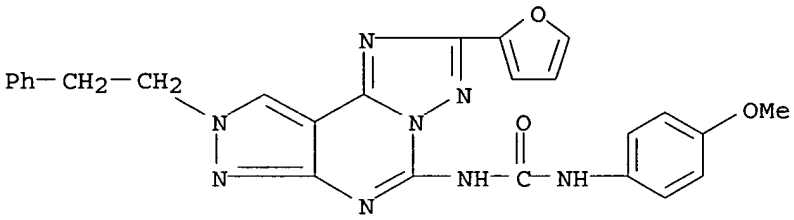
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



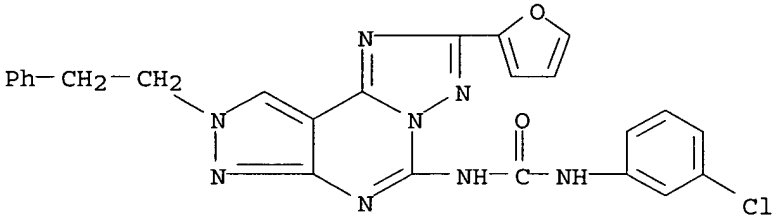
RN 252979-44-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



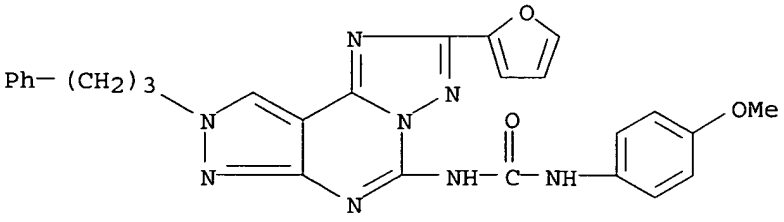
RN 252979-45-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 252979-46-7 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

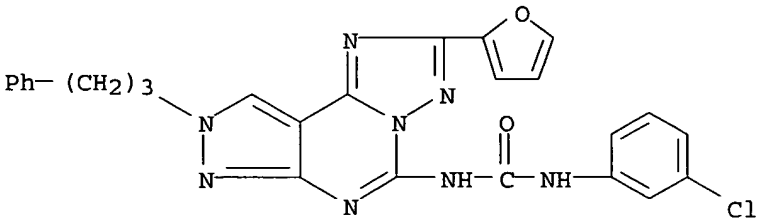


RN 252979-47-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

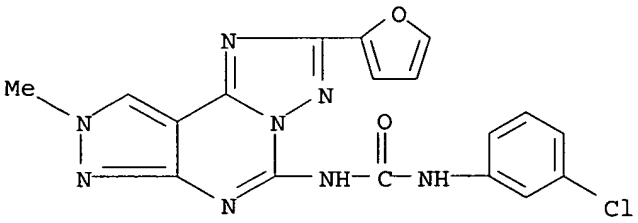


RN 252979-48-9 CAPLUS

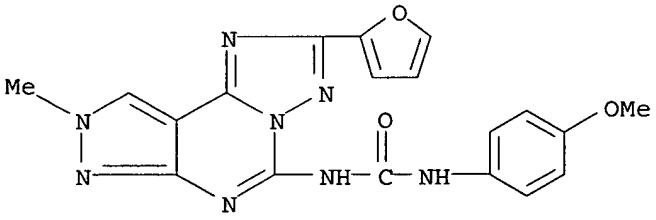
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



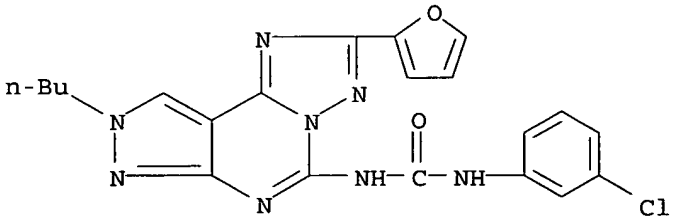
RN 261629-22-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



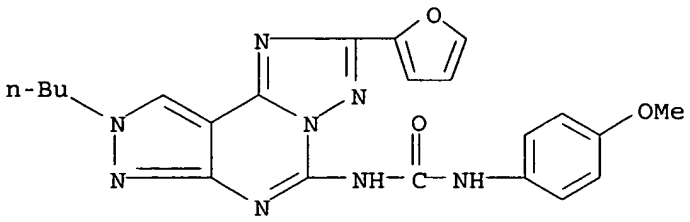
RN 261629-23-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



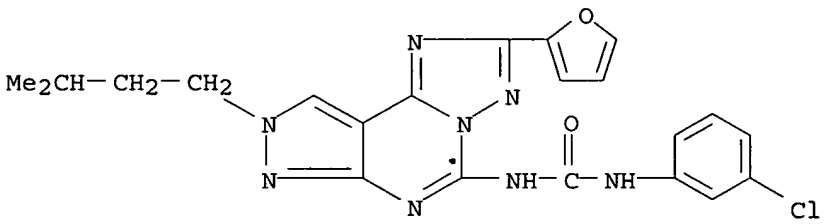
RN 261629-24-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



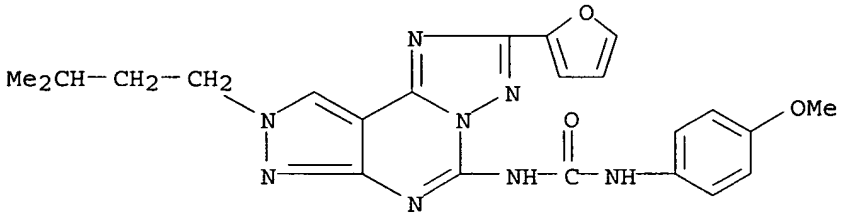
RN 261629-25-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



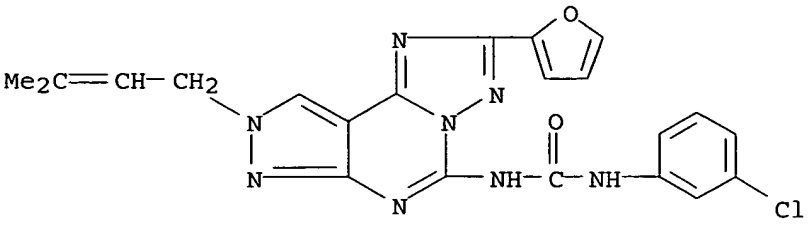
RN 261629-26-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



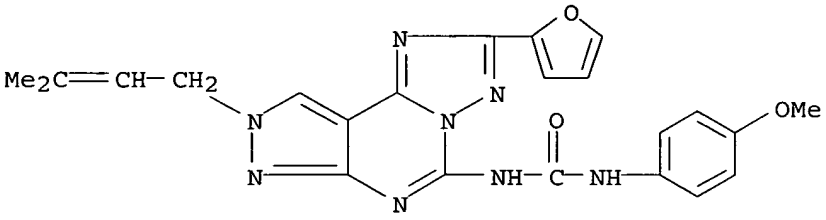
RN 261629-27-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



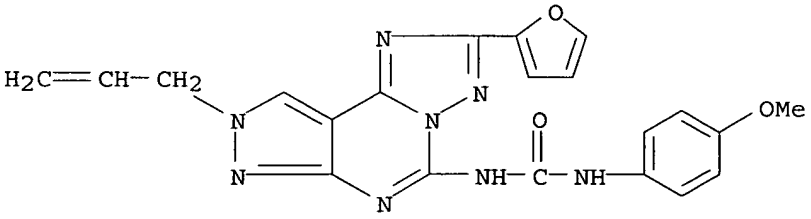
RN 261629-28-1 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



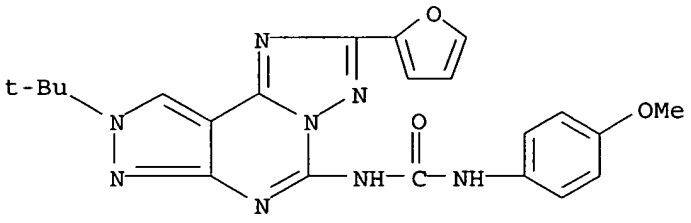
RN 261629-29-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 264623-54-3 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-propenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

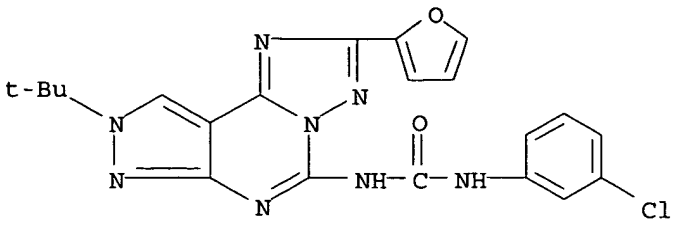


RN 321661-27-2 CAPLUS
CN Urea, N-[8-(1,1-dimethylethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

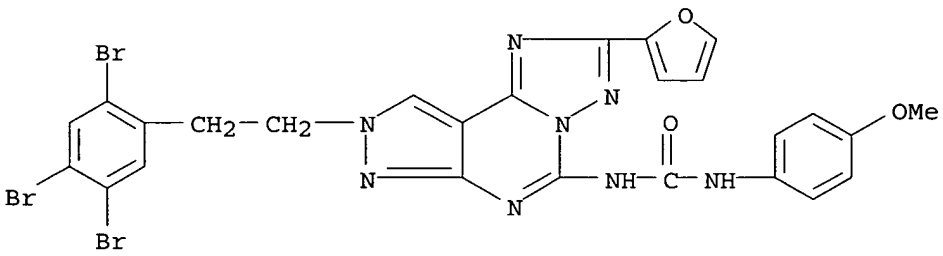


RN 321661-29-4 CAPLUS

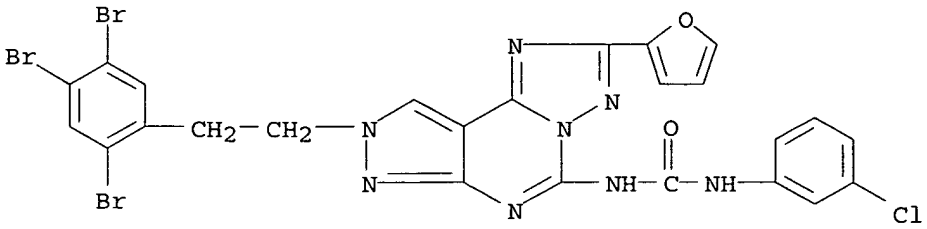
CN Urea, N-(3-chlorophenyl)-N'-[8-(1,1-dimethylethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 321661-35-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-[2-(2,4,5-tribromophenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

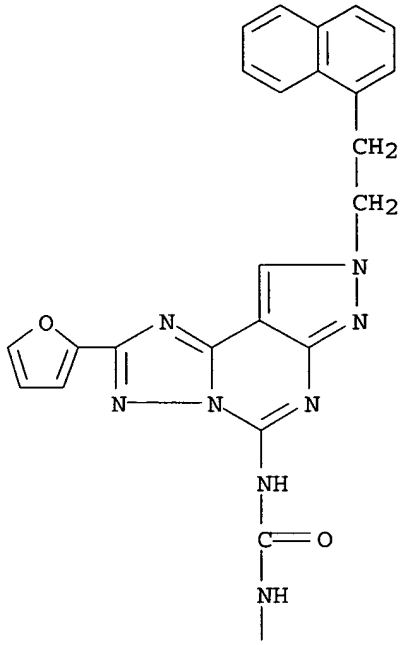


RN 321661-36-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-[2-(2,4,5-tribromophenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

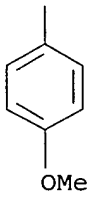


RN 321661-37-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-[2-(1-naphthalenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

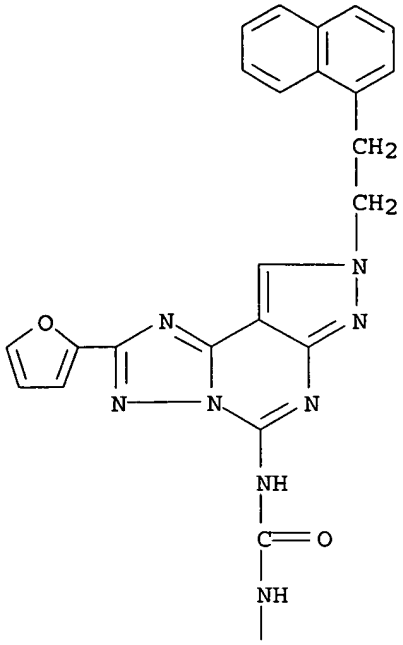


PAGE 2-A

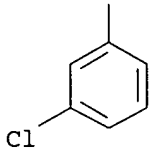


RN 321661-38-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-[2-(1-naphthalenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

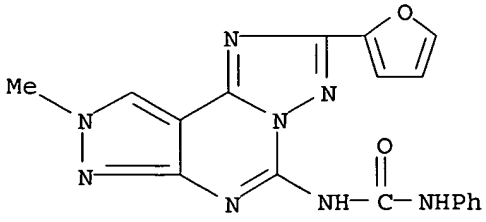
PAGE 1-A



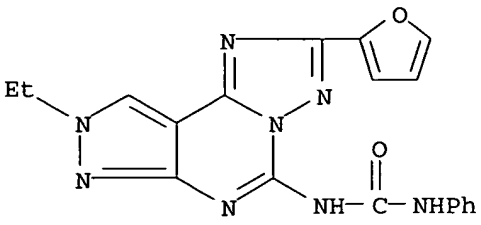
PAGE 2-A



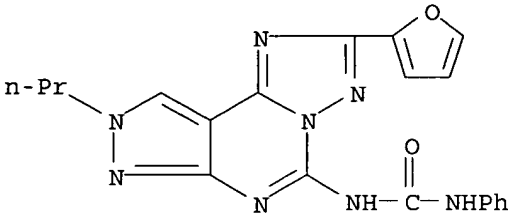
RN 361484-61-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



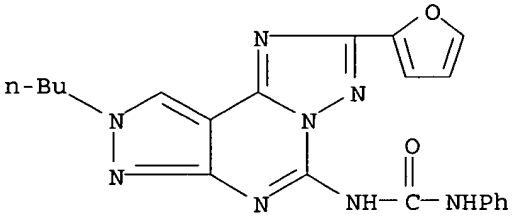
RN 361484-62-0 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



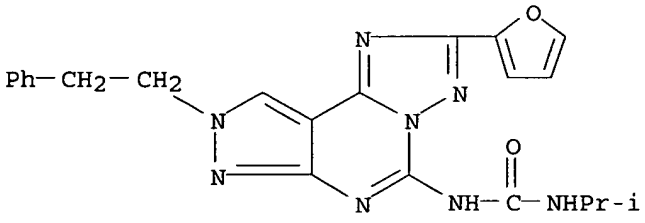
RN 361484-63-1 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



RN 361484-64-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)

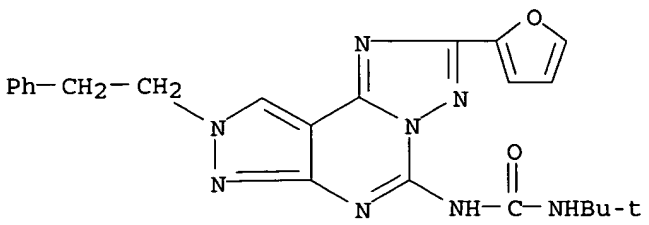


RN 385441-71-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

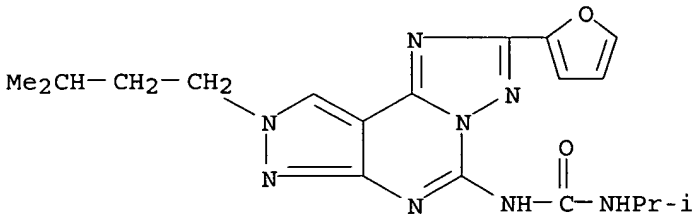


RN 385441-72-5 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX

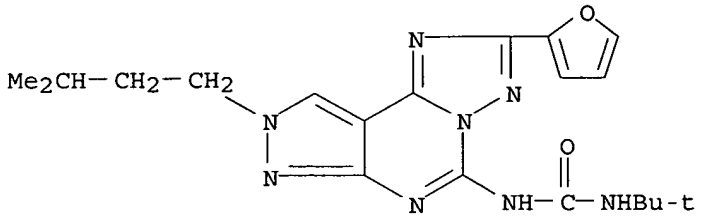
NAME)



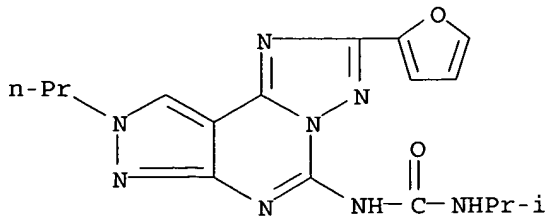
RN 385441-73-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



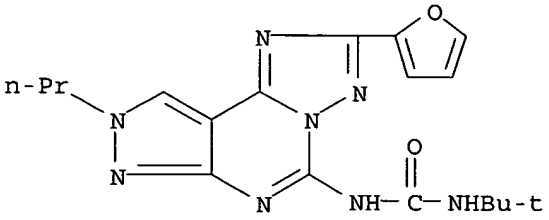
RN 385441-74-7 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



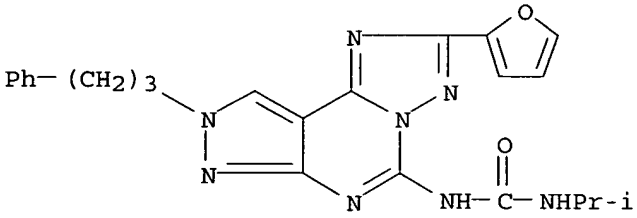
RN 385441-75-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



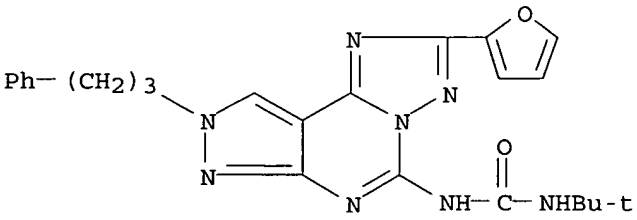
RN 385441-76-9 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



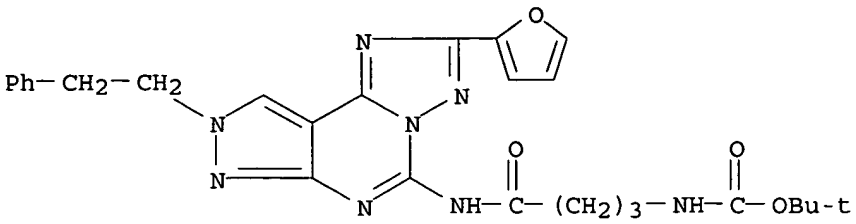
RN 385441-77-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



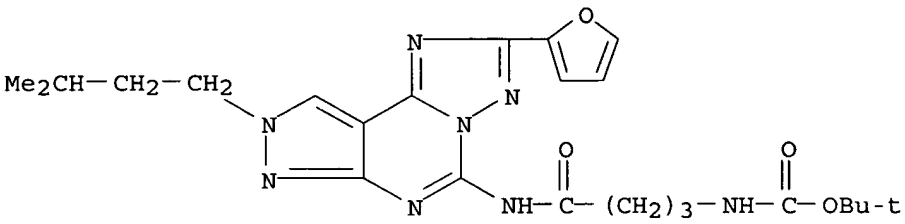
RN 385441-78-1 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



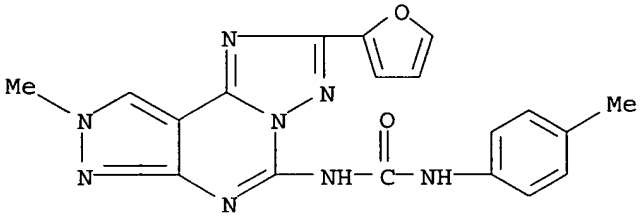
RN 385441-80-5 CAPLUS
CN Carbamic acid, [4-[[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]-4-oxobutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



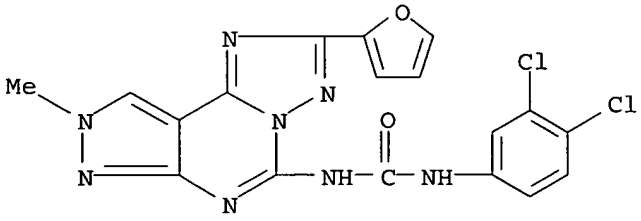
RN 385441-82-7 CAPLUS
CN Carbamic acid, [4-[[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]-4-oxobutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



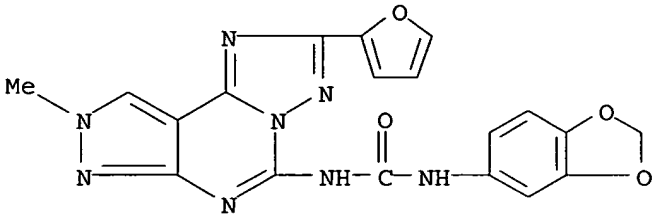
RN 396653-58-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



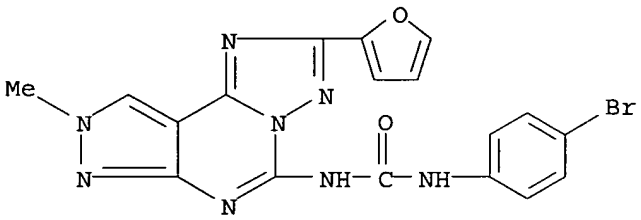
RN 404011-36-5 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



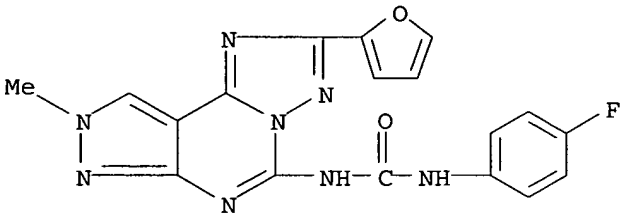
RN 404011-37-6 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



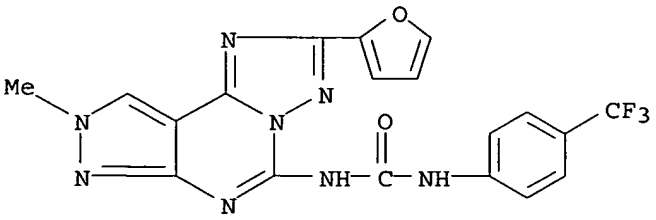
RN 404011-39-8 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 404011-40-1 CAPLUS
CN Urea, N-(4-fluorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

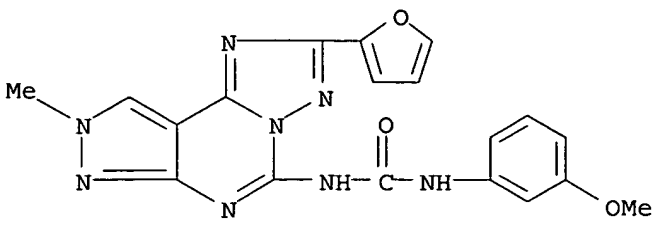


RN 404011-41-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

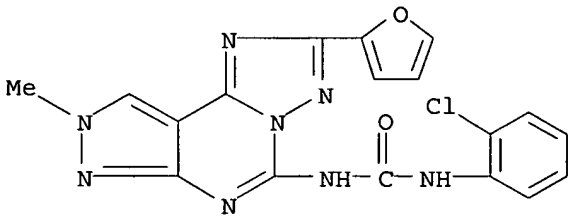


RN 404011-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-

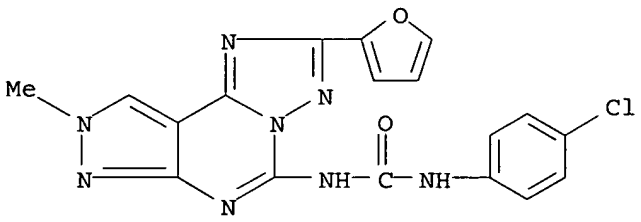
c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



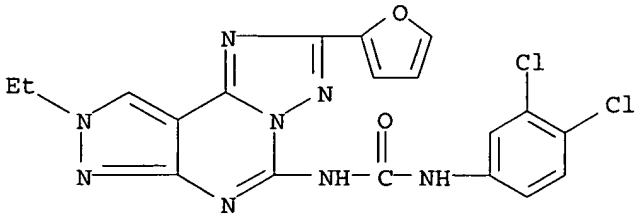
RN 404011-44-5 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 404011-45-6 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

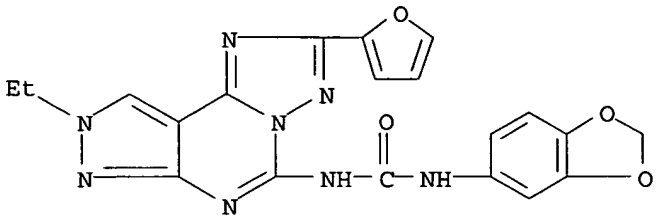


RN 404011-46-7 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

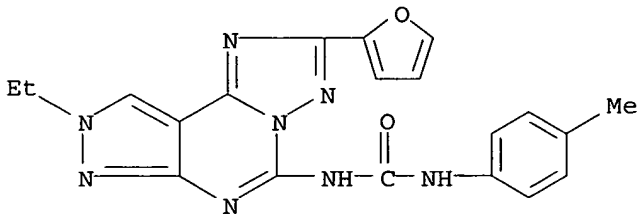


RN 404011-47-8 CAPLUS

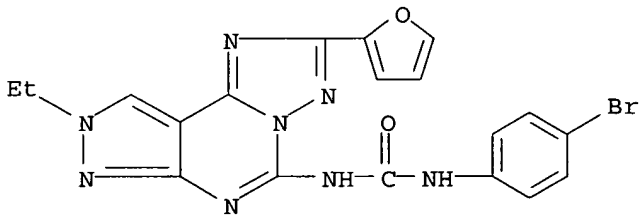
CN Urea, N-1,3-benzodioxol-5-yl-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



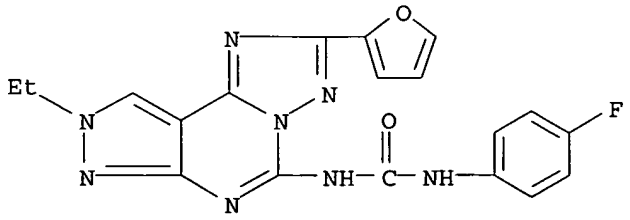
RN 404011-49-0 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



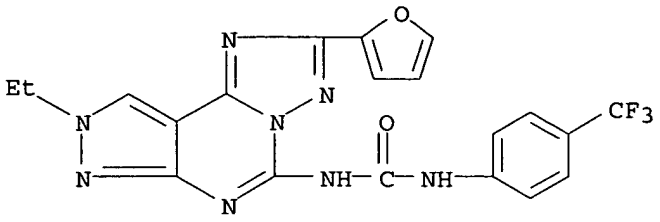
RN 404011-50-3 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



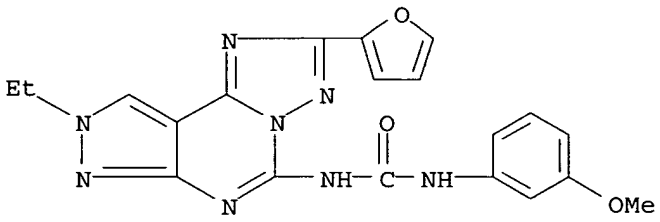
RN 404011-51-4 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



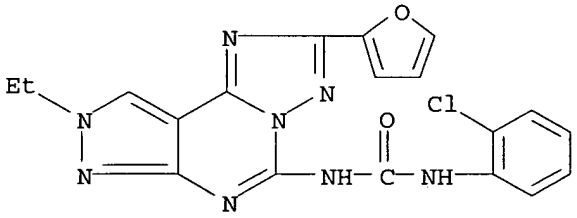
RN 404011-52-5 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



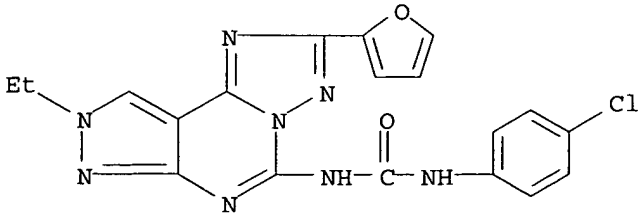
RN 404011-54-7 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



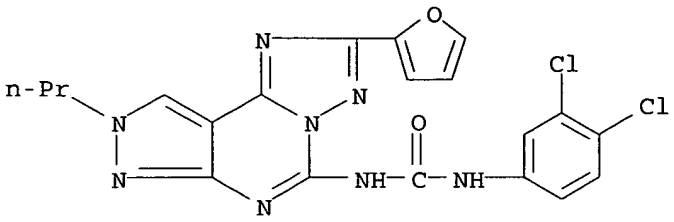
RN 404011-55-8 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



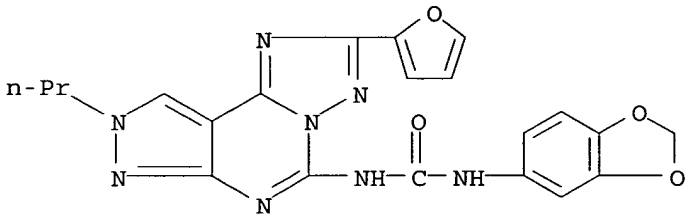
RN 404011-56-9 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



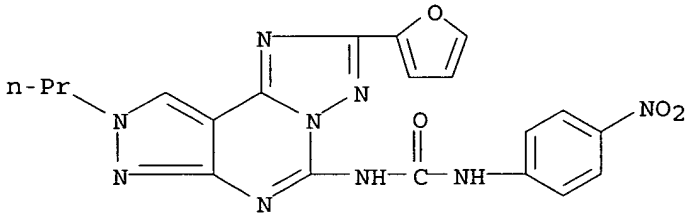
RN 404011-57-0 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



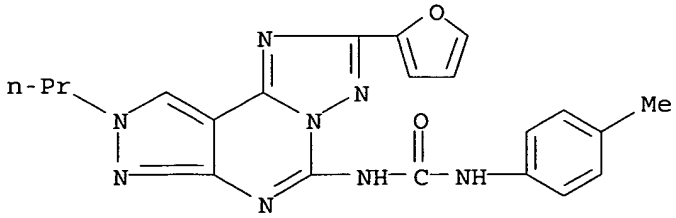
RN 404011-58-1 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



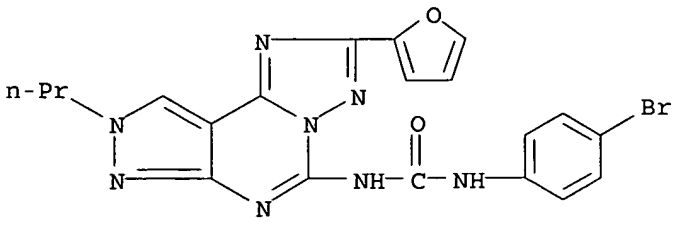
RN 404011-59-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



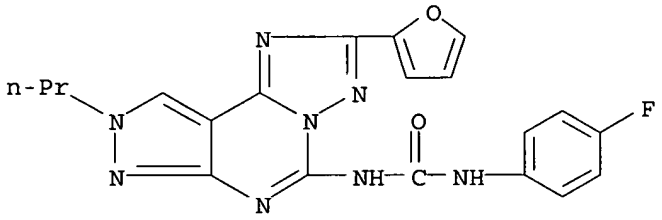
RN 404011-60-5 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



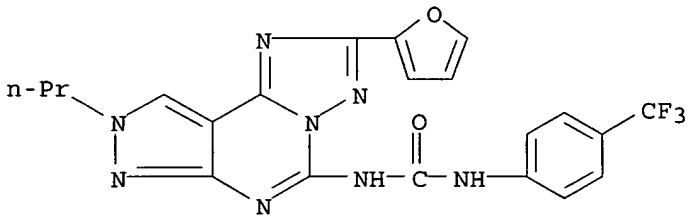
RN 404011-61-6 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



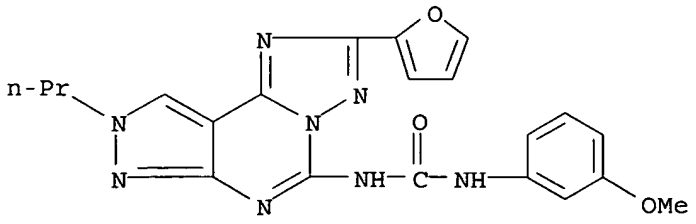
RN 404011-62-7 CAPLUS
CN Urea, N-(4-fluorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



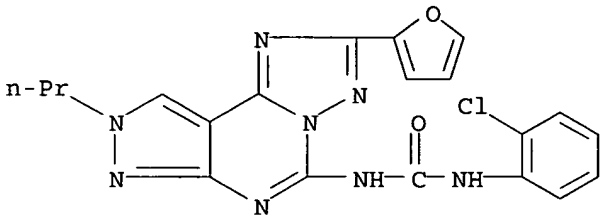
RN 404011-63-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



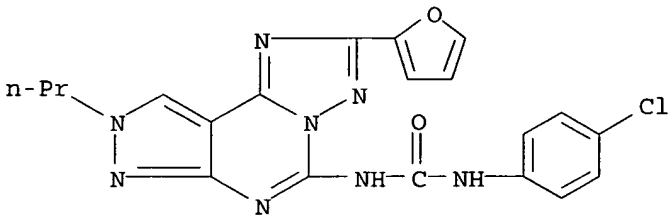
RN 404011-65-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



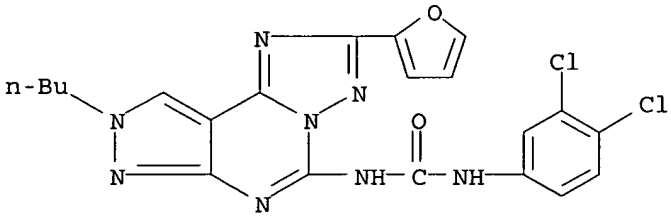
RN 404011-66-1 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



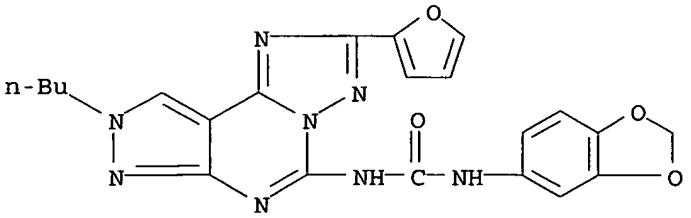
RN 404011-67-2 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



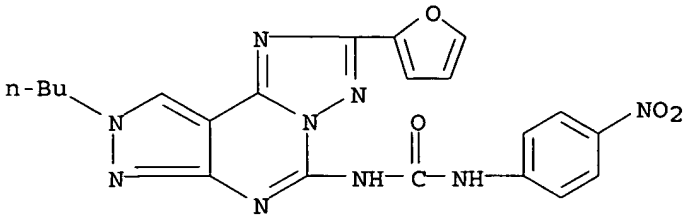
RN 404011-68-3 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



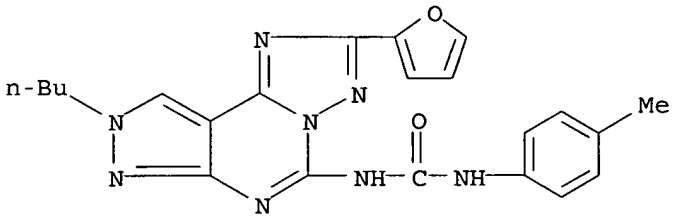
RN 404011-69-4 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



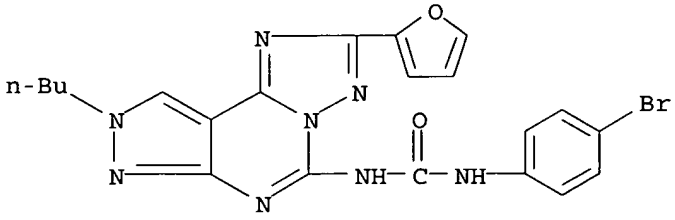
RN 404011-70-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



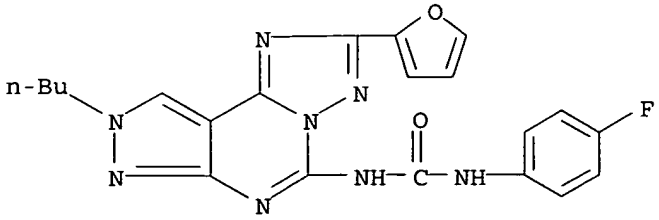
RN 404011-71-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



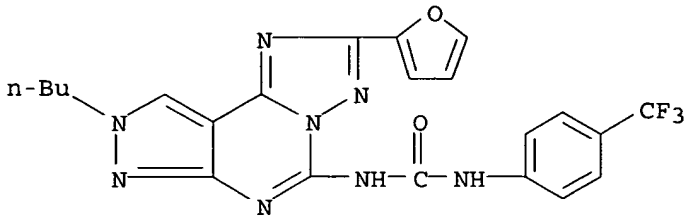
RN 404011-72-9 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



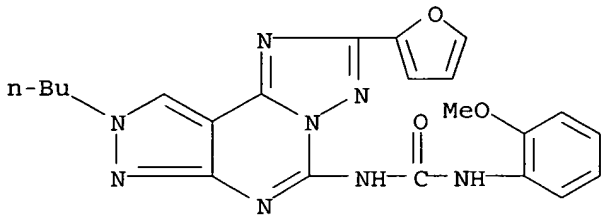
RN 404011-73-0 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



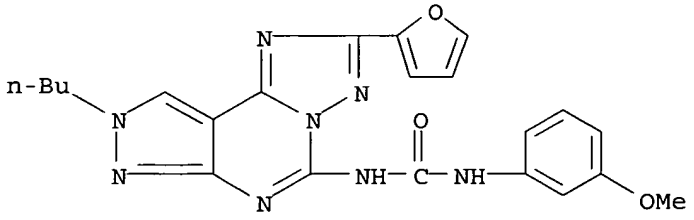
RN 404011-74-1 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



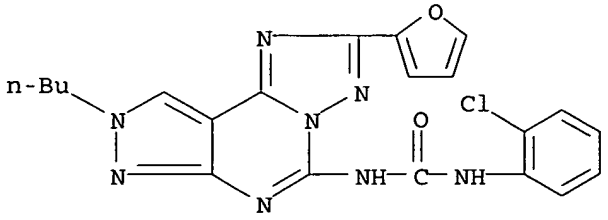
RN 404011-75-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



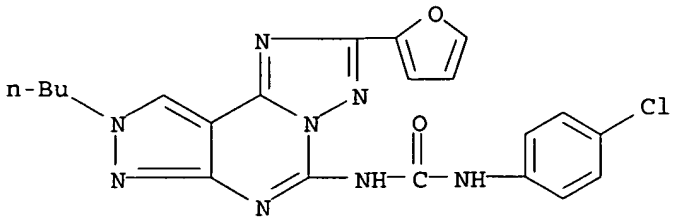
RN 404011-76-3 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



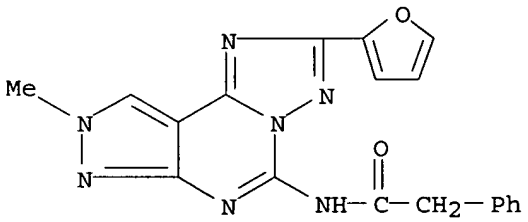
RN 404011-77-4 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-chlorophenyl)- (9CI) (CA INDEX NAME)



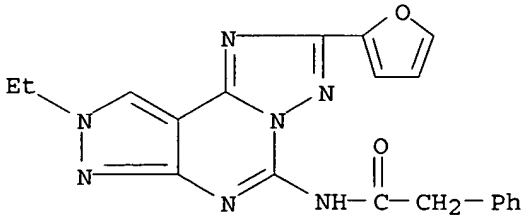
RN 404011-78-5 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



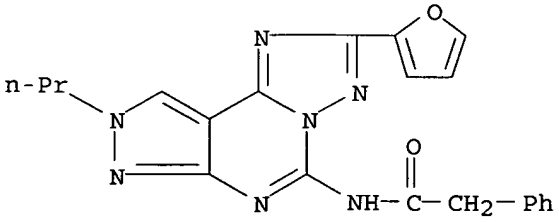
RN 404011-79-6 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



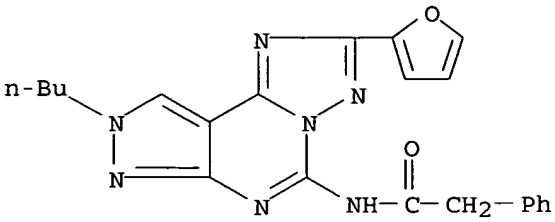
RN 404011-80-9 CAPLUS
CN Benzeneacetamide, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



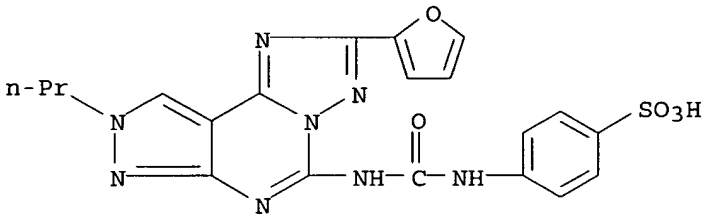
RN 404011-81-0 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



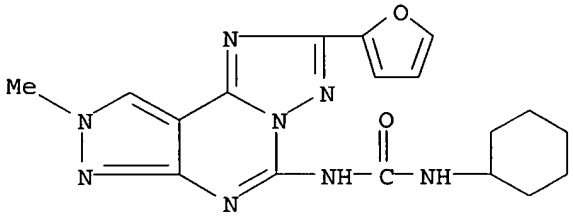
RN 404011-82-1 CAPLUS
CN Benzeneacetamide, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



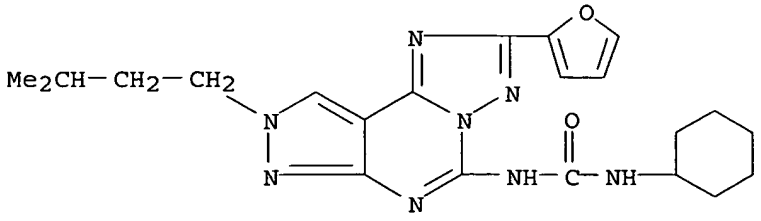
RN 404011-85-4 CAPLUS
CN Benzenesulfonic acid, 4-[[[[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



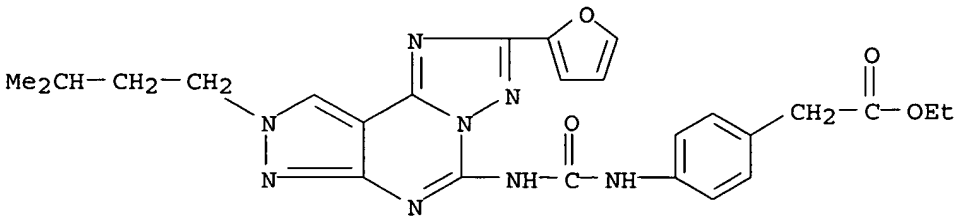
RN 827629-36-7 CAPLUS
CN Urea, N-cyclohexyl-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



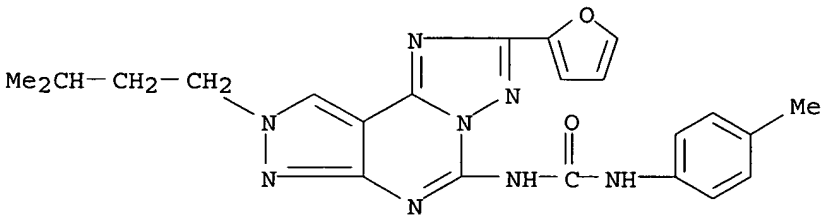
RN 827629-39-0 CAPLUS
CN Urea, N-cyclohexyl-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



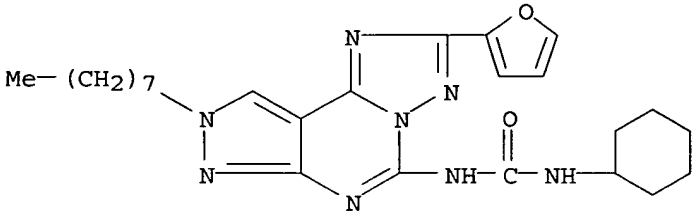
RN 827629-41-4 CAPLUS
CN Benzeneacetic acid, 4-[[[[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



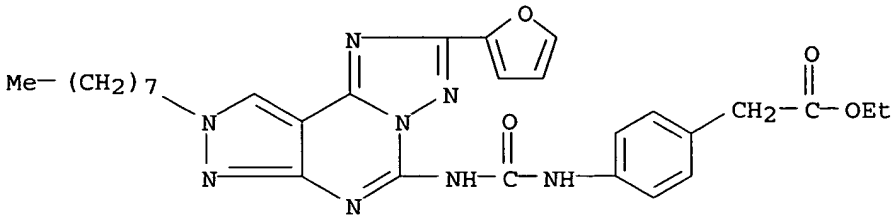
RN 827629-42-5 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



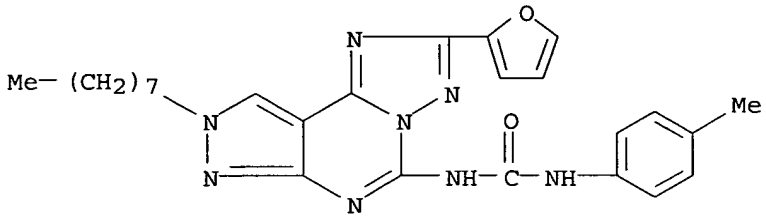
RN 827629-43-6 CAPLUS
CN Urea, N-cyclohexyl-N'-[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



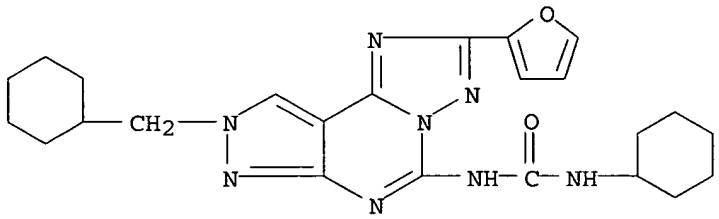
RN 827629-45-8 CAPLUS
CN Benzeneacetic acid, 4-[[[[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



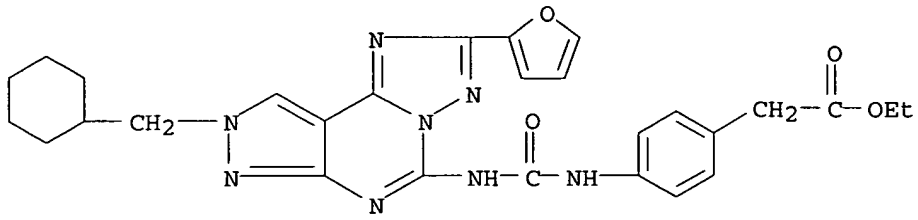
RN 827629-46-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



RN 827629-47-0 CAPLUS
CN Urea, N-cyclohexyl-N'-[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

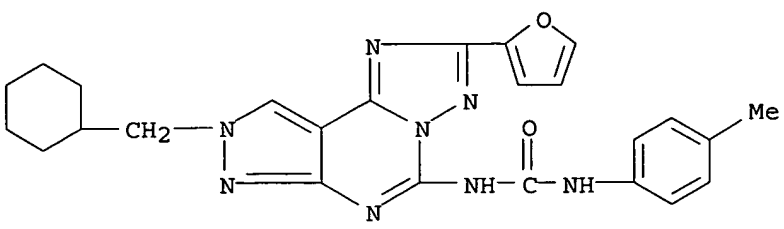


RN 827629-49-2 CAPLUS
CN Benzeneacetic acid, 4-[[[[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

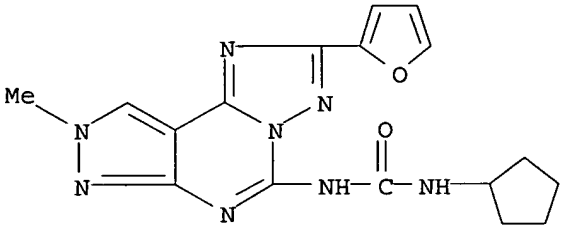


RN 827629-50-5 CAPLUS
CN Urea, N-[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA

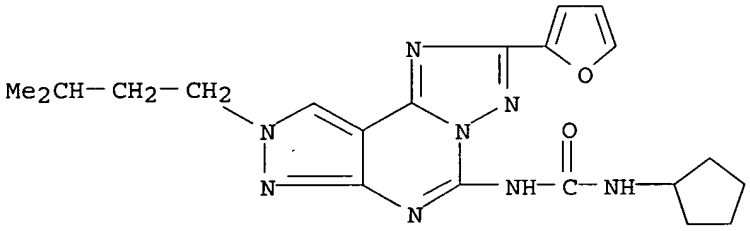
INDEX NAME)



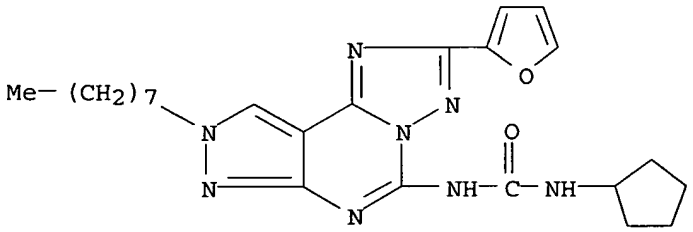
RN 865788-07-4 CAPLUS
CN Urea, N-cyclopentyl-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 865788-08-5 CAPLUS
CN Urea, N-cyclopentyl-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

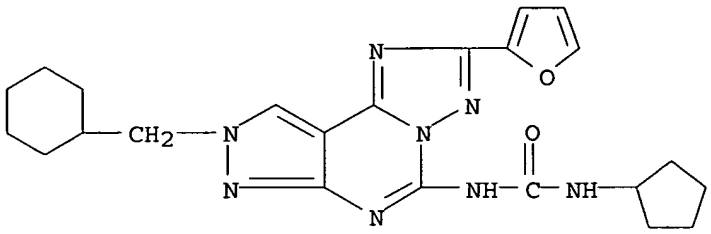


RN 865788-09-6 CAPLUS
CN Urea, N-cyclopentyl-N'-[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 865788-10-9 CAPLUS

CN Urea, N-[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-cyclopentyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

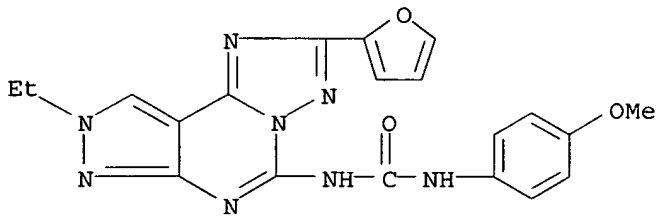
L6 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:260970 CAPLUS
DOCUMENT NUMBER: 143:19235
TITLE: Autocorrelation of Molecular Electrostatic Potential surface properties combined with partial least squares analysis as alternative attractive tool to generate ligand-based 3D-QSARs
AUTHOR(S): Moro, Stefano; Bacilieri, Magdalena; Ferrari, Cristina; Spalluto, Giampiero
CORPORATE SOURCE: Molecular Modeling Section, Dipartimento di Scienze Farmaceutiche, Universita di Padova, Padua, I-35131, Italy
SOURCE: Current Drug Discovery Technologies (2005), 2(1), 13-21
CODEN: CDDTAF; ISSN: 1570-1638
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A database of 106 human A3 adenosine receptor antagonists was used to derive two alternative PLS models: one starting from CoMFA descriptors and the other starting from the autocorrelation descriptors. The peculiarity of this work is the introduction of autocorrelation vectors as mol. descriptors for the PLS anal. The autocorrelation allows comparing mols. (and their properties) with different structures and with different spatial orientation without any previous alignment. In particular, Mol. Electrostatic Potential (MEP) was the property computed and its information encoded in autocorrelation vectors. The 3D spatial distribution and the values of the electrostatic potential is in fact largely responsible for the binding of a substrate to its receptor binding site. Validation was done with an external test set and the results of the two models were compared. Interestingly, our preliminary results seem to indicate that this new alternative approach could robustly compete with the already well consolidated CoMFA approach. In particular, we have suggested that it could be a very interesting tool to filter large structural database in several virtual screening applications.

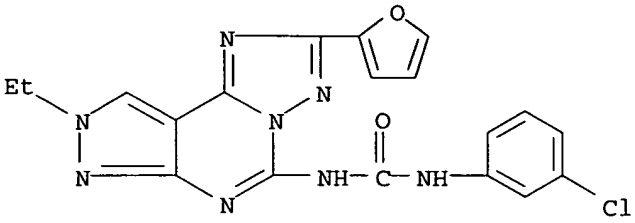
IT **252979-41-2 252979-42-3 252979-43-4**
252979-44-5 252979-45-6 252979-46-7
252979-47-8 252979-48-9 261629-22-5
261629-23-6 261629-24-7 261629-25-8
261629-26-9 261629-27-0 261629-28-1
261629-29-2 264623-54-3 321661-16-9

321661-18-1 321661-27-2 321661-29-4
321661-35-2 321661-36-3 321661-37-4
321661-38-5 361484-61-9 361484-62-0
361484-63-1 361484-64-2 385441-71-4
385441-72-5 385441-73-6 385441-74-7
385441-75-8 385441-76-9 385441-77-0
385441-78-1 385441-79-2 385441-80-5
385441-81-6 385441-82-7 385441-86-1
396653-58-0 404011-36-5 404011-37-6
404011-38-7 404011-39-8 404011-40-1
404011-41-2 404011-42-3 404011-43-4
404011-44-5 404011-45-6 404011-46-7
404011-47-8 404011-48-9 404011-49-0
404011-50-3 404011-51-4 404011-52-5
404011-53-6 404011-54-7 404011-55-8
404011-56-9 404011-57-0 404011-58-1
404011-59-2 404011-60-5 404011-61-6
404011-62-7 404011-63-8 404011-64-9
404011-65-0 404011-66-1 404011-67-2
404011-68-3 404011-69-4 404011-70-7
404011-71-8 404011-72-9 404011-73-0
404011-74-1 404011-75-2 404011-76-3
404011-77-4 404011-78-5 404011-79-6
404011-80-9 404011-81-0 404011-82-1
827629-36-7 827629-37-8 827629-38-9
827629-39-0 827629-40-3 827629-41-4
827629-42-5 827629-43-6 827629-44-7
827629-45-8 827629-46-9 827629-47-0
827629-48-1 827629-49-2 827629-50-5
852676-85-8
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(autocorrelation of mol. Electrostatic Potential surface properties combined with partial least squares anal. as alternative attractive tool to generate ligand-based 3D-QSARs)

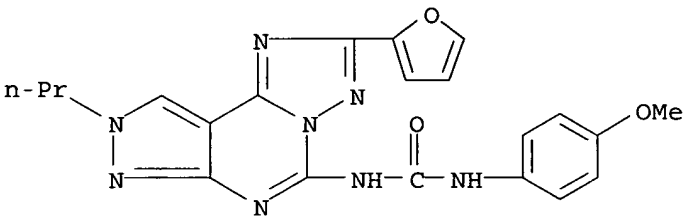
RN 252979-41-2 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



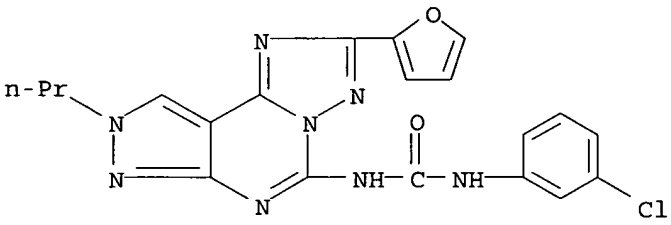
RN 252979-42-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



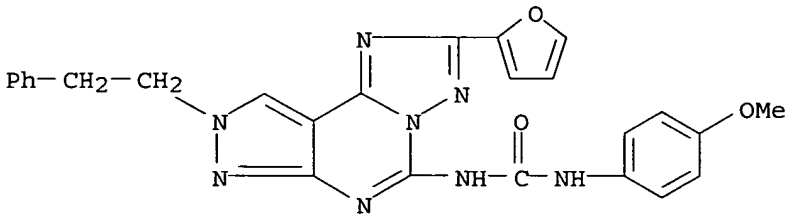
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 252979-44-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

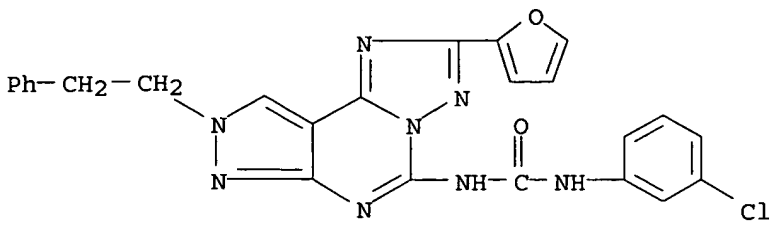


RN 252979-45-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

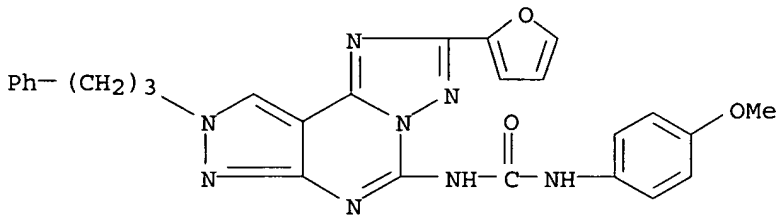


RN 252979-46-7 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX

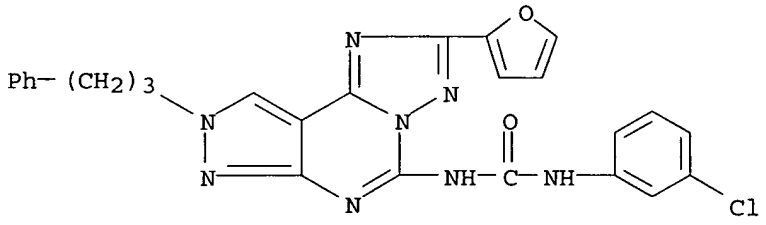
NAME)



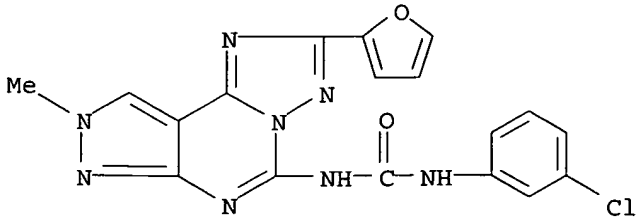
RN 252979-47-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



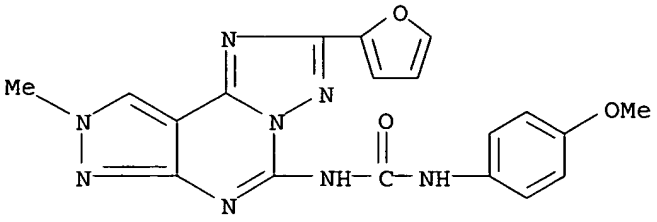
RN 252979-48-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



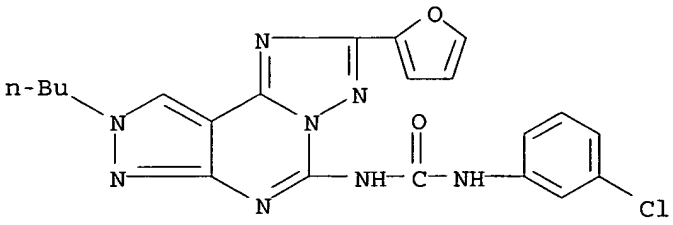
RN 261629-22-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



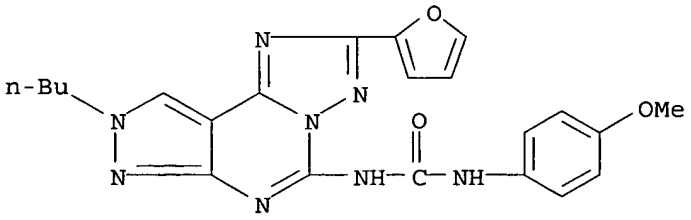
RN 261629-23-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



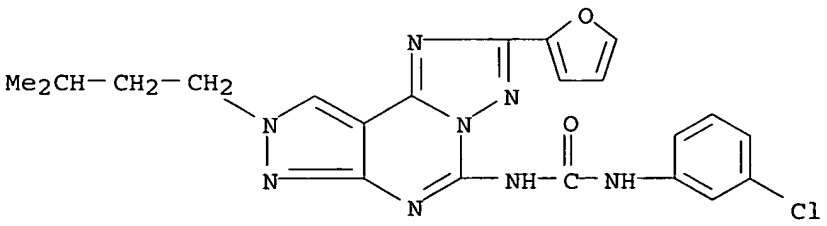
RN 261629-24-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



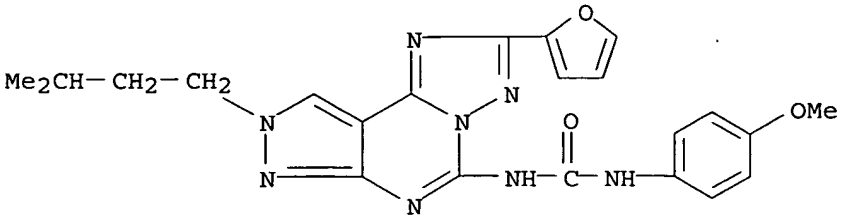
RN 261629-25-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



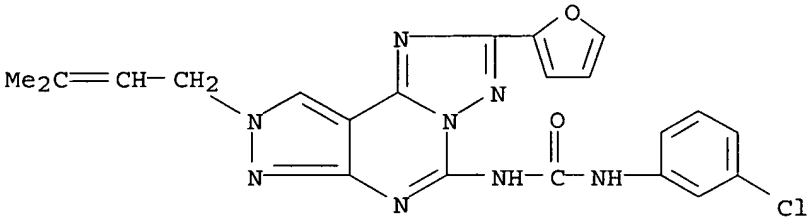
RN 261629-26-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



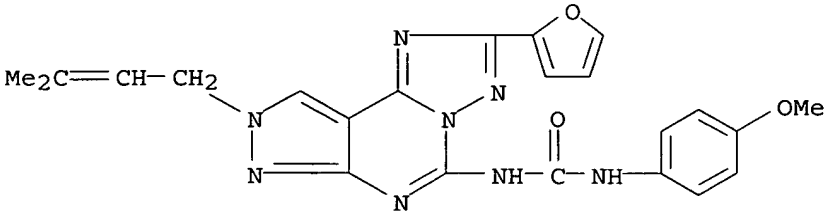
RN 261629-27-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



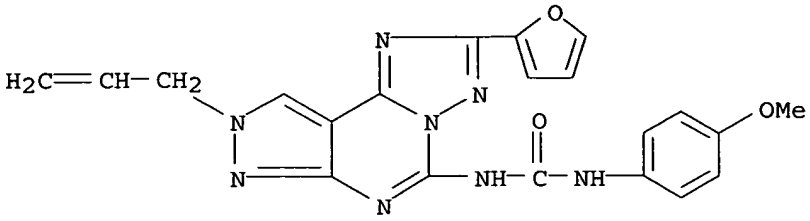
RN 261629-28-1 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



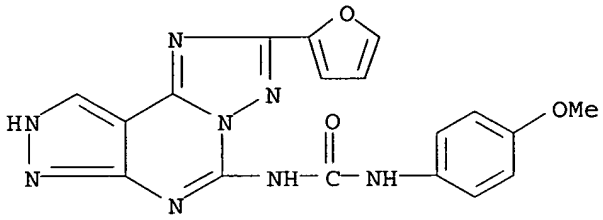
RN 261629-29-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



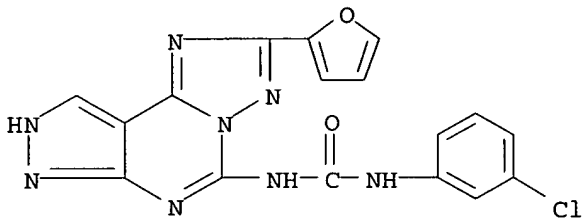
RN 264623-54-3 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-propenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



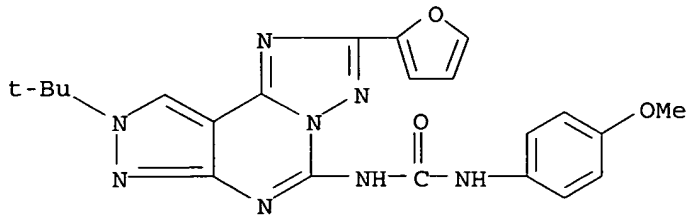
RN 321661-16-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 321661-18-1 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

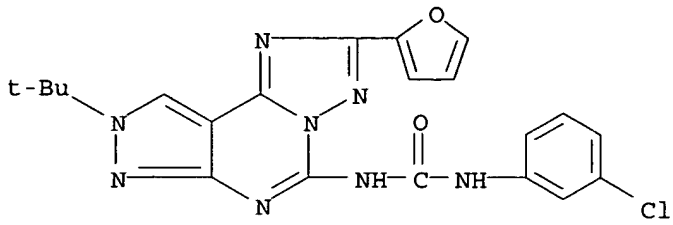


RN 321661-27-2 CAPLUS
CN Urea, N-[8-(1,1-dimethylethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

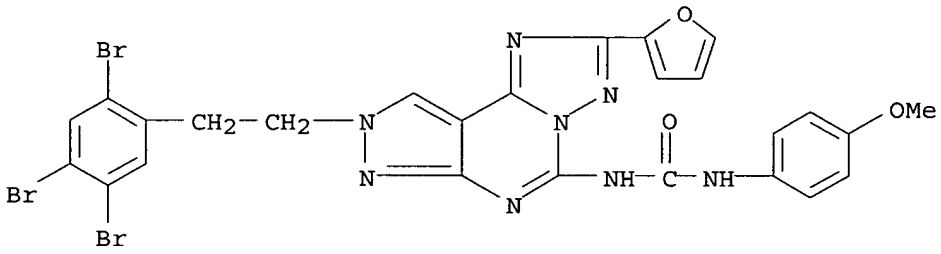


RN 321661-29-4 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-(1,1-dimethylethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX

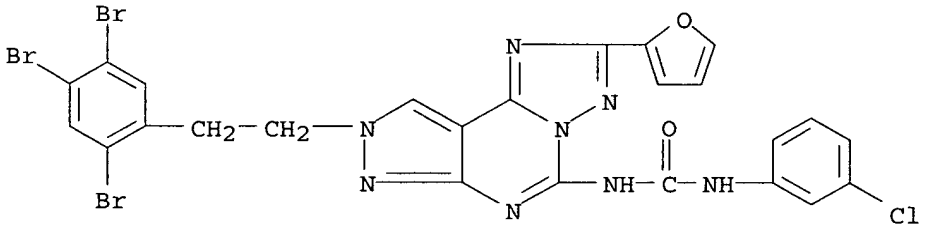
NAME)



RN 321661-35-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-[2-(2,4,5-tribromophenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

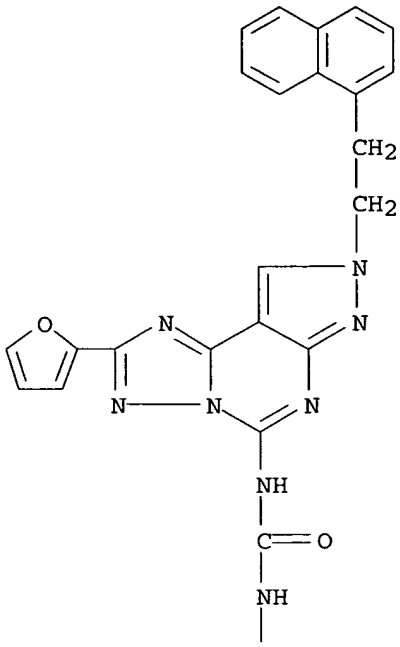


RN 321661-36-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-[2-(2,4,5-tribromophenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

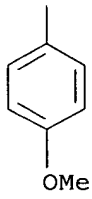


RN 321661-37-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-[2-(1-naphthalenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

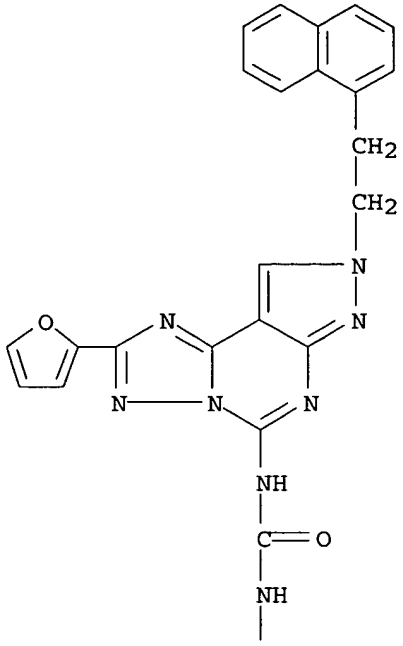


PAGE 2-A

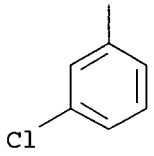


RN 321661-38-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-[2-(1-naphthalenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

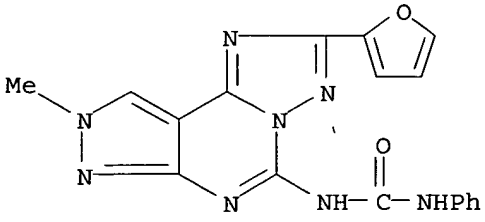
PAGE 1-A



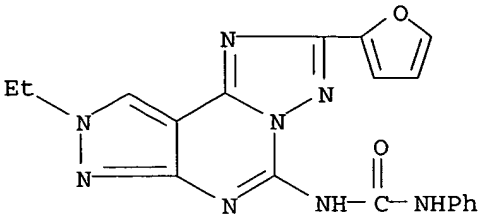
PAGE 2-A



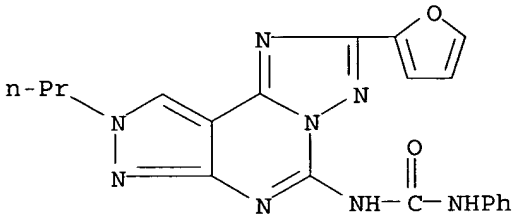
RN 361484-61-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



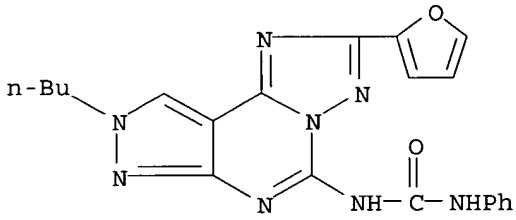
RN 361484-62-0 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



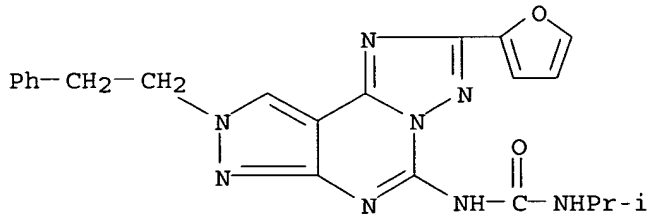
RN 361484-63-1 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



RN 361484-64-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)

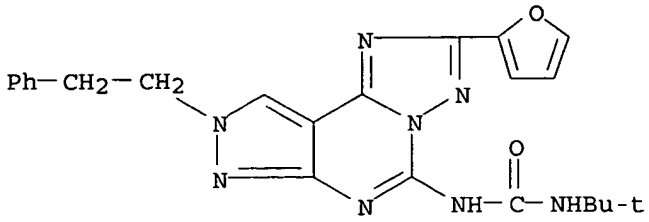


RN 385441-71-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

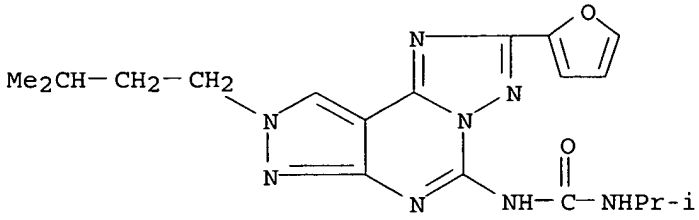


RN 385441-72-5 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX

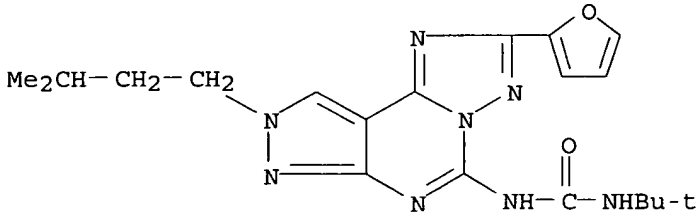
NAME)



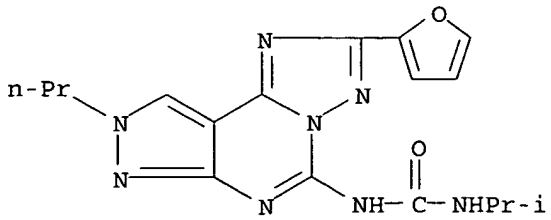
RN 385441-73-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



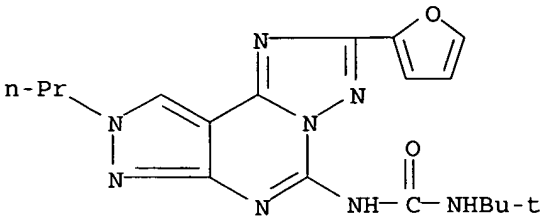
RN 385441-74-7 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



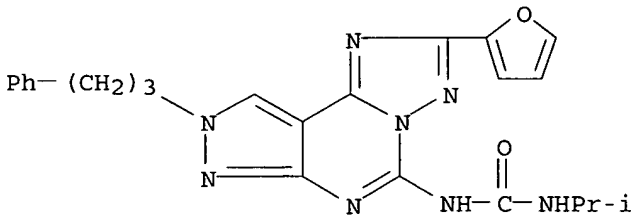
RN 385441-75-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



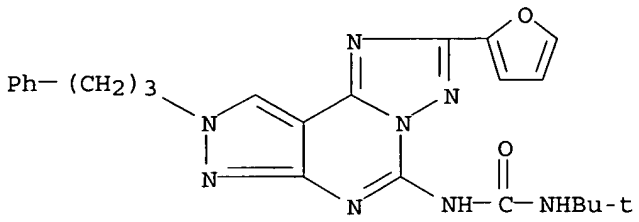
RN 385441-76-9 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



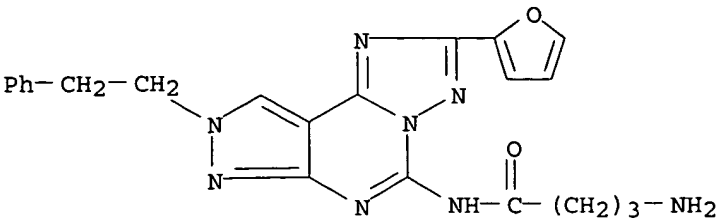
RN 385441-77-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 385441-78-1 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

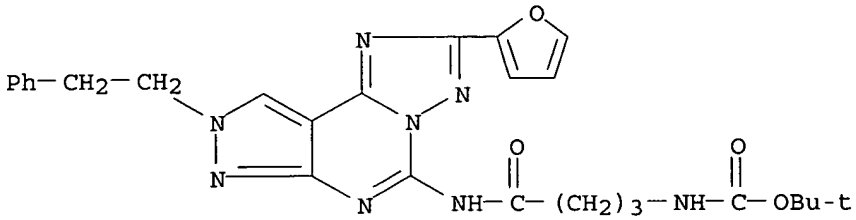


RN 385441-79-2 CAPLUS
CN Butanamide, 4-amino-N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

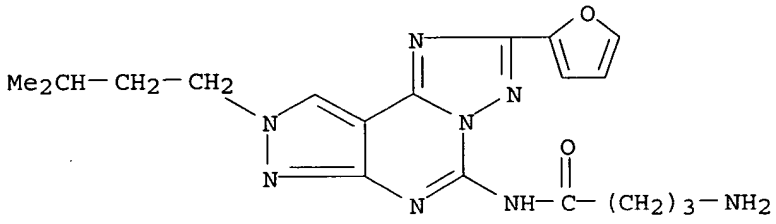


● HCl

RN 385441-80-5 CAPLUS
CN Carbamic acid, [4-[[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]-4-oxobutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

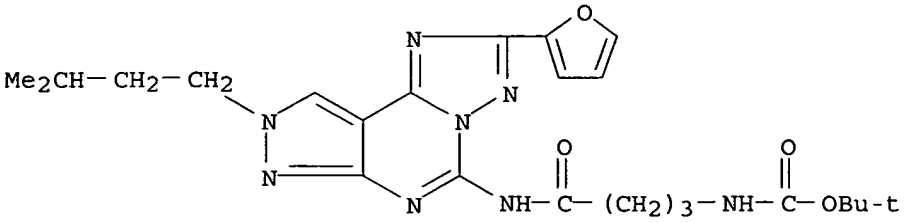


RN 385441-81-6 CAPLUS
CN Butanamide, 4-amino-N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

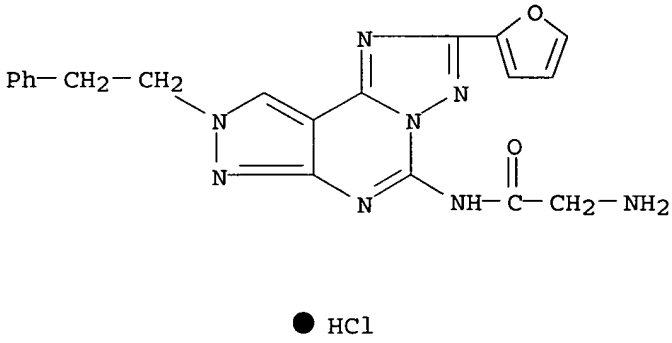


● HCl

RN 385441-82-7 CAPLUS
CN Carbamic acid, [4-[[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]-4-oxobutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

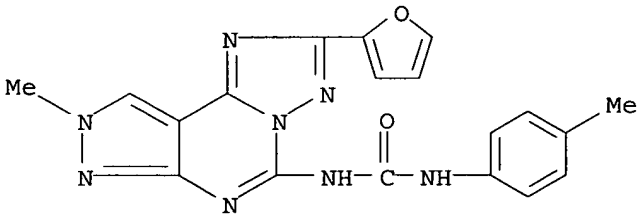


RN 385441-86-1 CAPLUS
CN Acetamide, 2-amino-N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

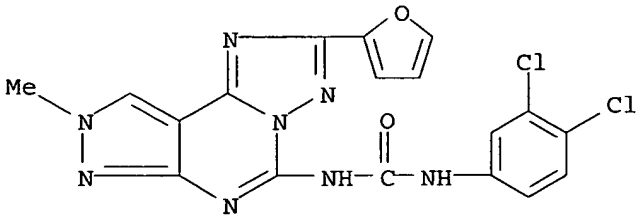


● HCl

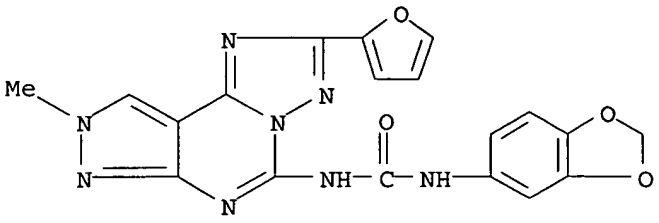
RN 396653-58-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



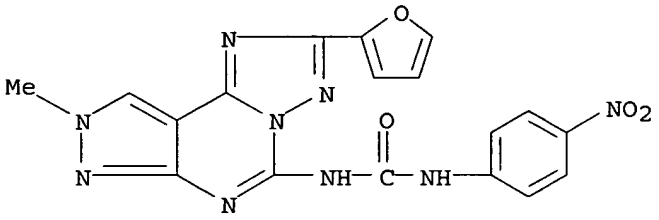
RN 404011-36-5 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



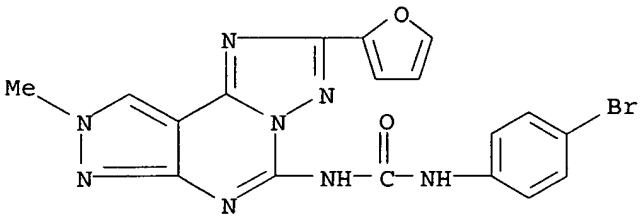
RN 404011-37-6 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



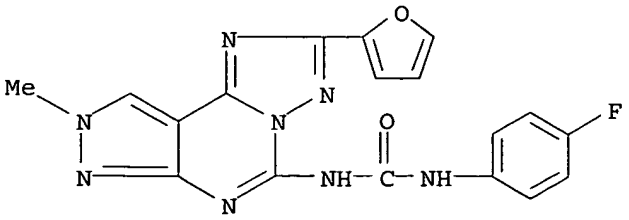
RN 404011-38-7 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



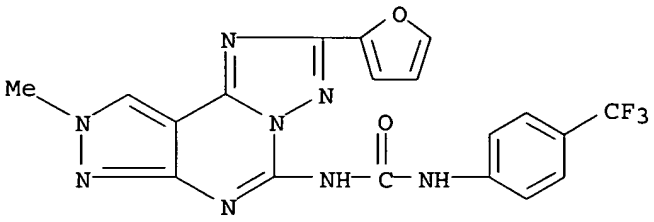
RN 404011-39-8 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



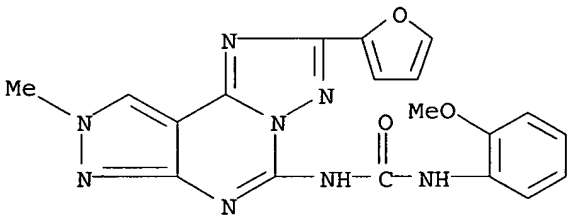
RN 404011-40-1 CAPLUS
CN Urea, N-(4-fluorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



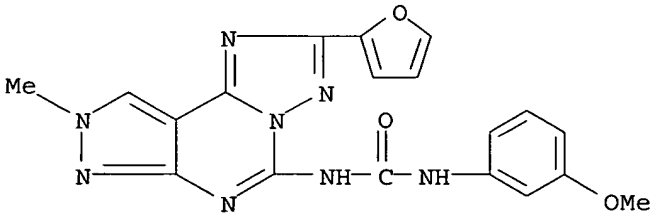
RN 404011-41-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



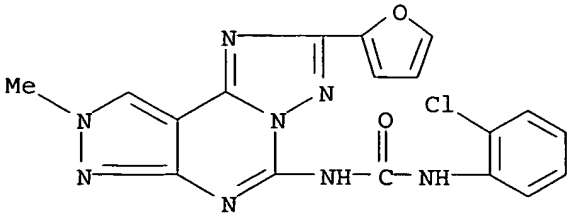
RN 404011-42-3 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



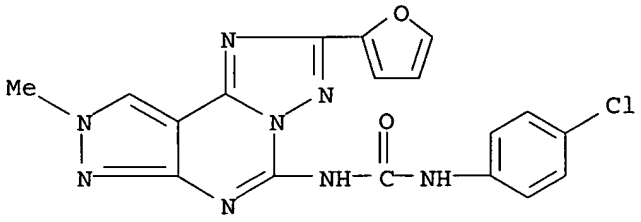
RN 404011-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



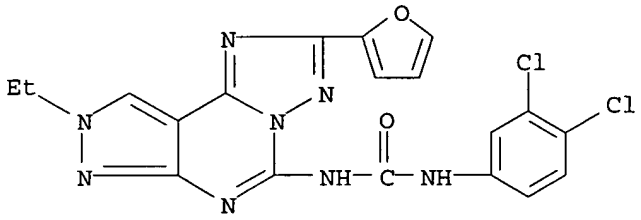
RN 404011-44-5 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



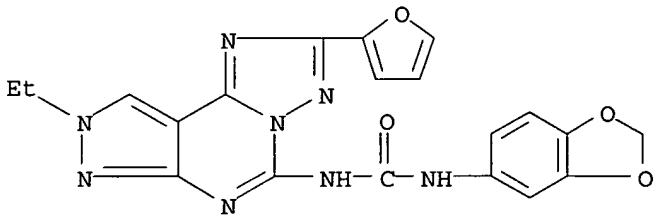
RN 404011-45-6 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



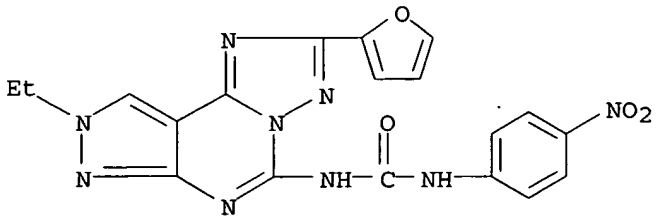
RN 404011-46-7 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



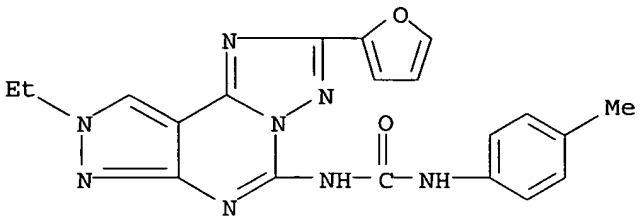
RN 404011-47-8 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



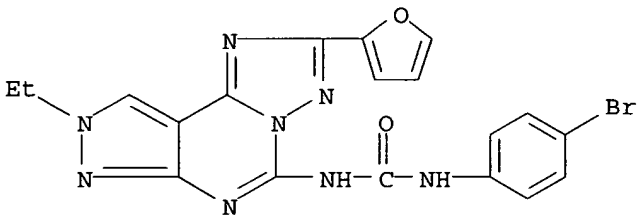
RN 404011-48-9 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



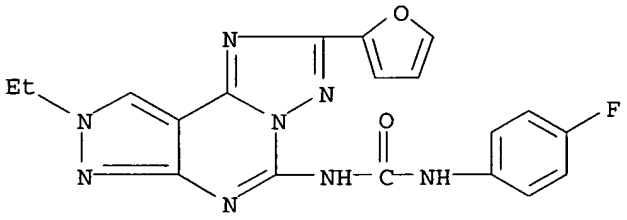
RN 404011-49-0 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



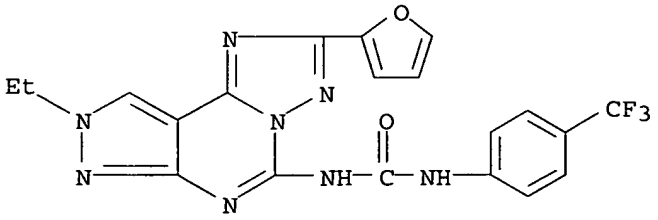
RN 404011-50-3 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



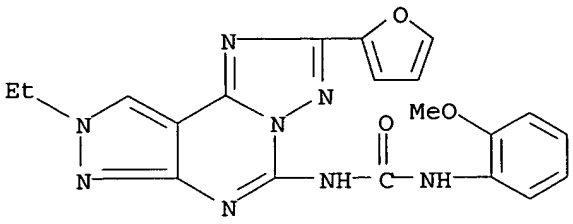
RN 404011-51-4 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



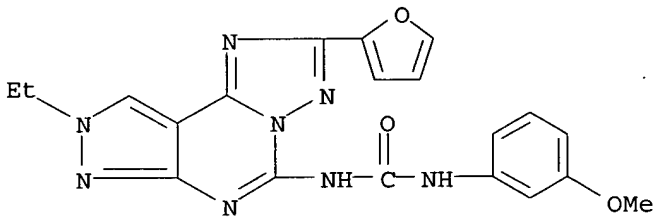
RN 404011-52-5 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



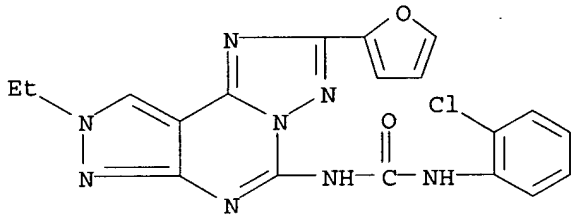
RN 404011-53-6 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



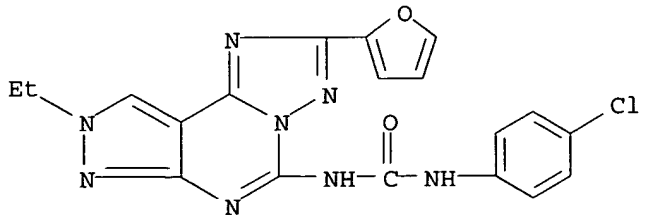
RN 404011-54-7 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



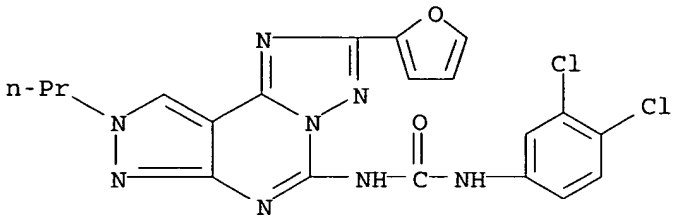
RN 404011-55-8 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



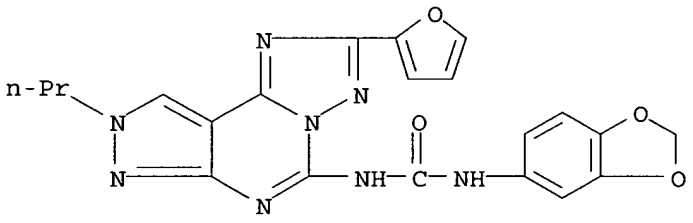
RN 404011-56-9 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



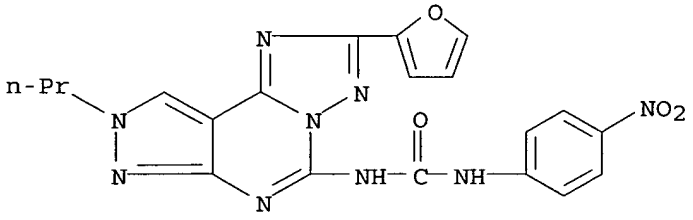
RN 404011-57-0 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



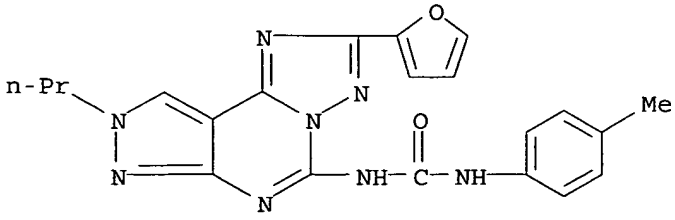
RN 404011-58-1 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



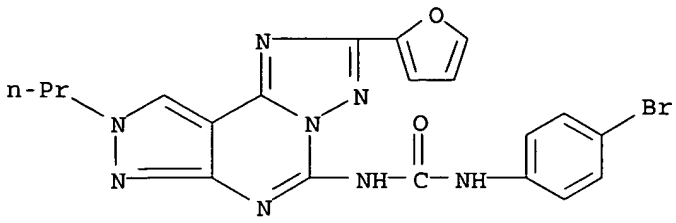
RN 404011-59-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



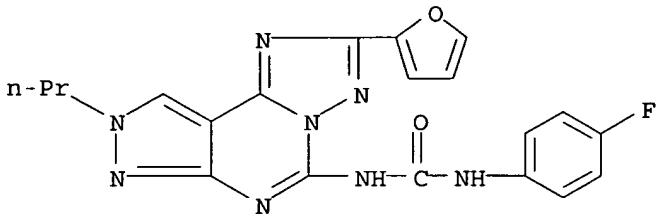
RN 404011-60-5 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



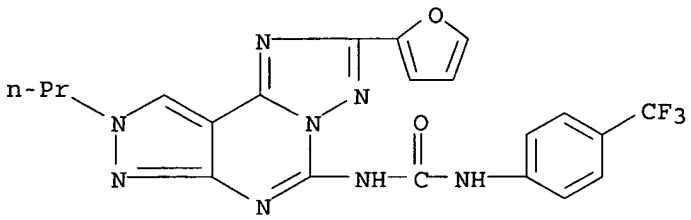
RN 404011-61-6 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



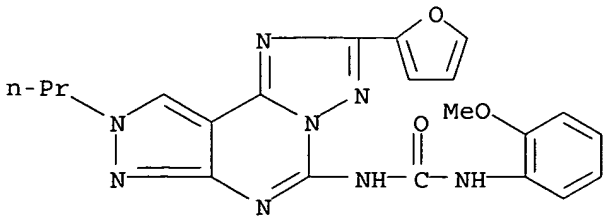
RN 404011-62-7 CAPLUS
CN Urea, N-(4-fluorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



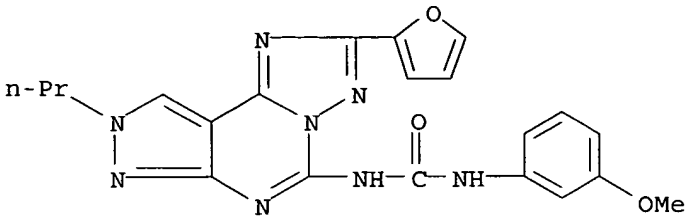
RN 404011-63-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



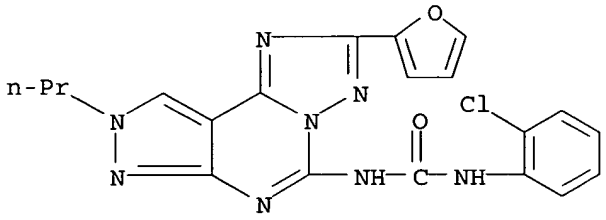
RN 404011-64-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



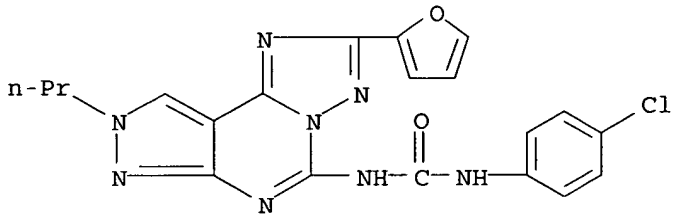
RN 404011-65-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



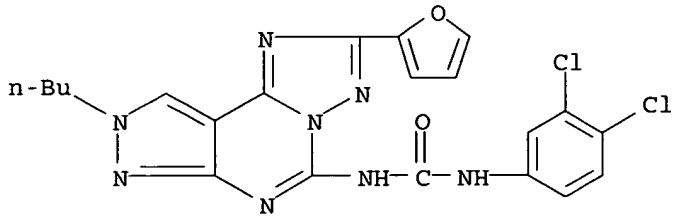
RN 404011-66-1 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



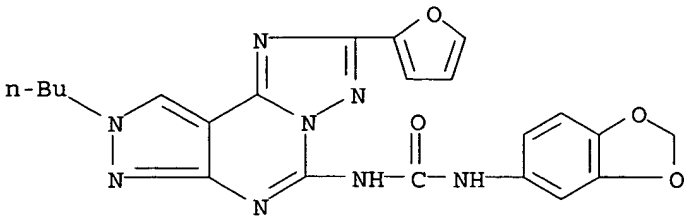
RN 404011-67-2 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



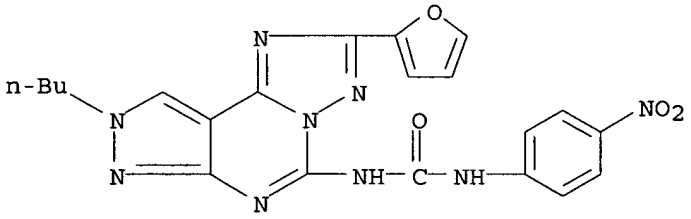
RN 404011-68-3 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



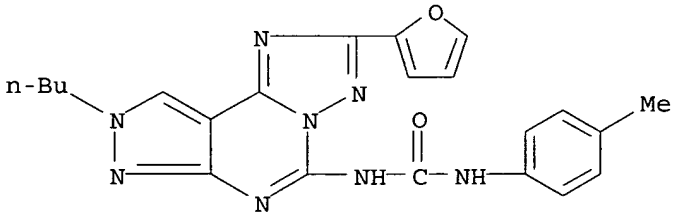
RN 404011-69-4 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



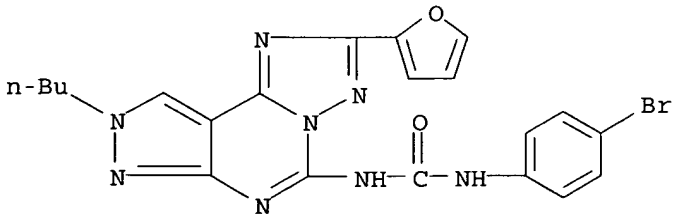
RN 404011-70-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



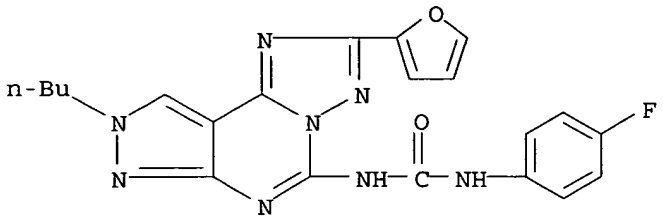
RN 404011-71-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



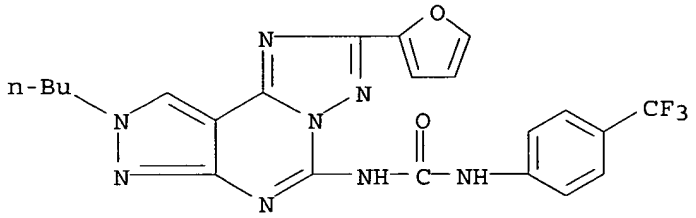
RN 404011-72-9 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



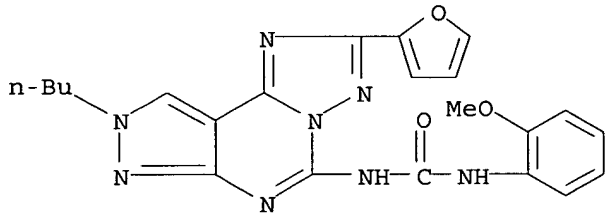
RN 404011-73-0 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



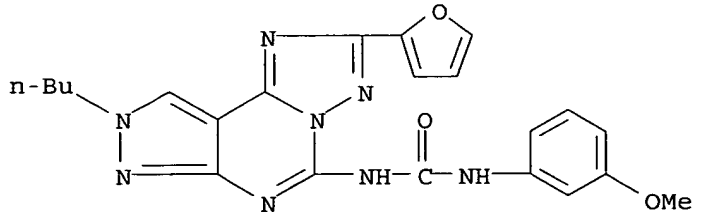
RN 404011-74-1 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



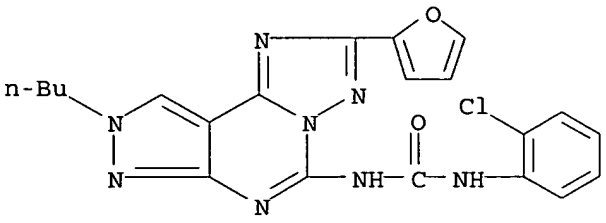
RN 404011-75-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



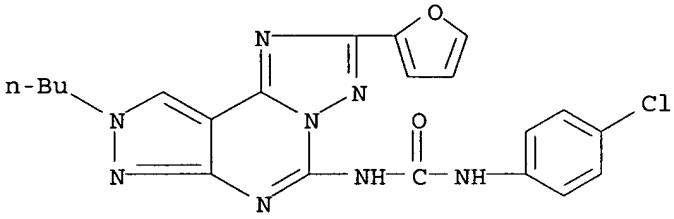
RN 404011-76-3 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



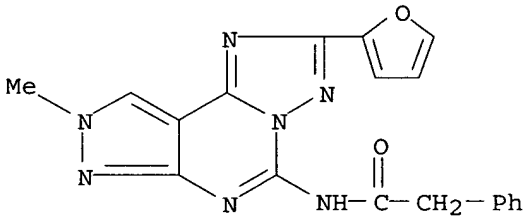
RN 404011-77-4 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-chlorophenyl)- (9CI) (CA INDEX NAME)



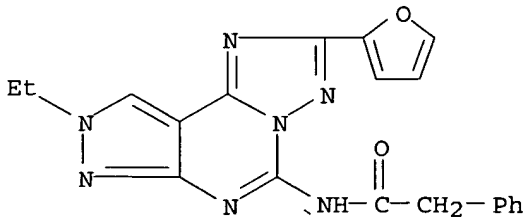
RN 404011-78-5 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



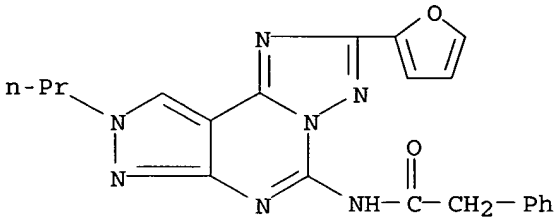
RN 404011-79-6 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



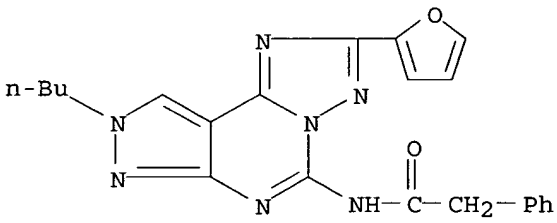
RN 404011-80-9 CAPLUS
CN Benzeneacetamide, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



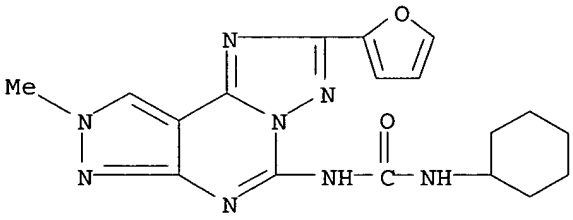
RN 404011-81-0 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



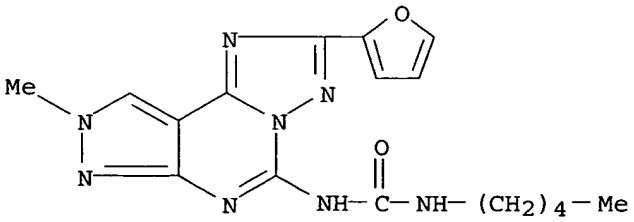
RN 404011-82-1 CAPLUS
CN Benzeneacetamide, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



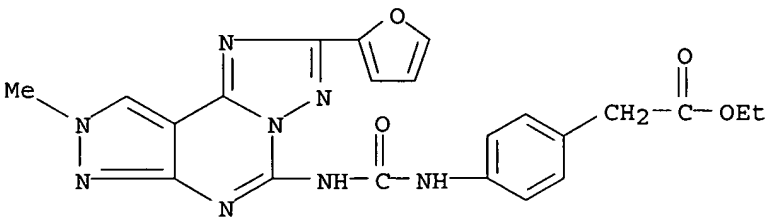
RN 827629-36-7 CAPLUS
CN Urea, N-cyclohexyl-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



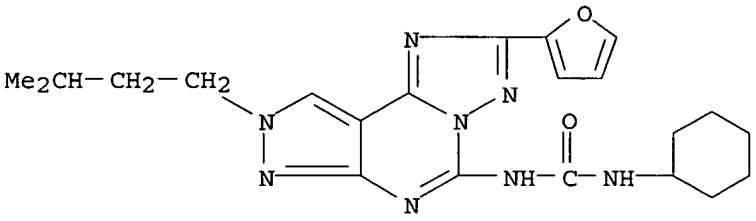
RN 827629-37-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-pentyl- (9CI) (CA INDEX NAME)



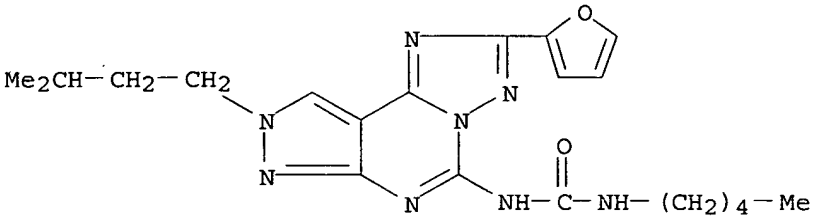
RN 827629-38-9 CAPLUS
CN Benzeneacetic acid, 4-[[[[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



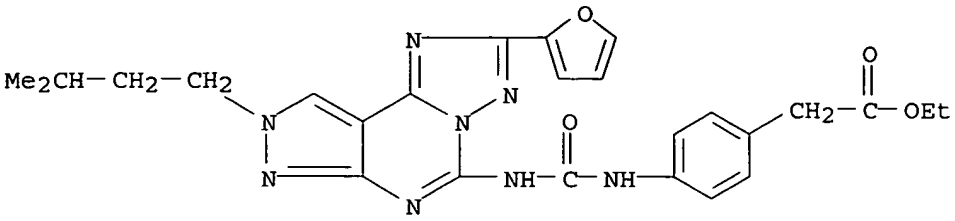
RN 827629-39-0 CAPLUS
CN Urea, N-cyclohexyl-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



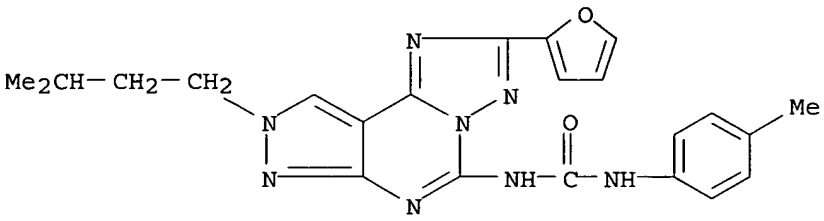
RN 827629-40-3 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-pentyl- (9CI) (CA INDEX NAME)



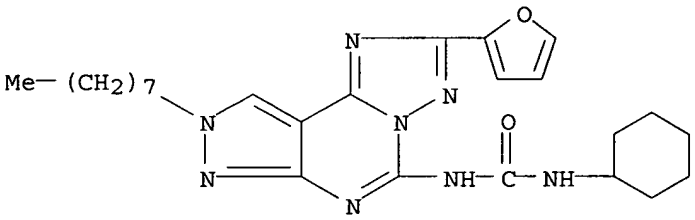
RN 827629-41-4 CAPLUS
CN Benzeneacetic acid, 4-[[[[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



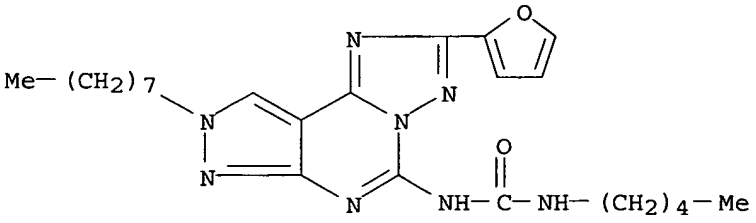
RN 827629-42-5 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



RN 827629-43-6 CAPLUS
CN Urea, N-cyclohexyl-N'-[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

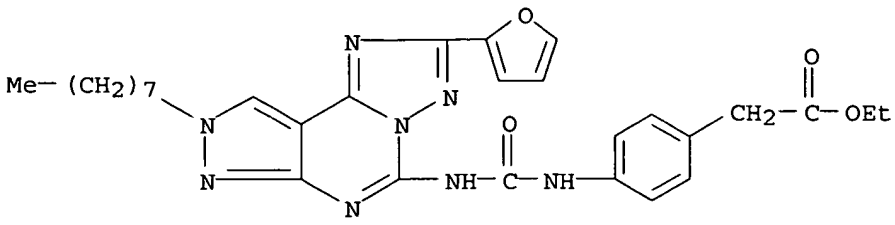


RN 827629-44-7 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-pentyl- (9CI) (CA INDEX NAME)

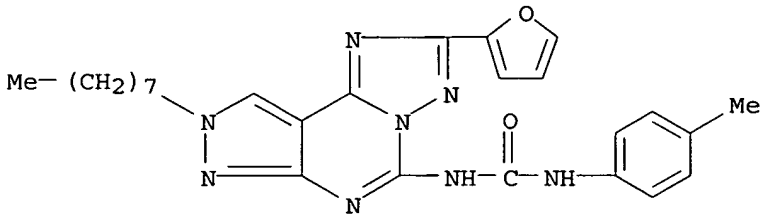


RN 827629-45-8 CAPLUS
CN Benzeneacetic acid, 4-[[[[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-, ethyl ester

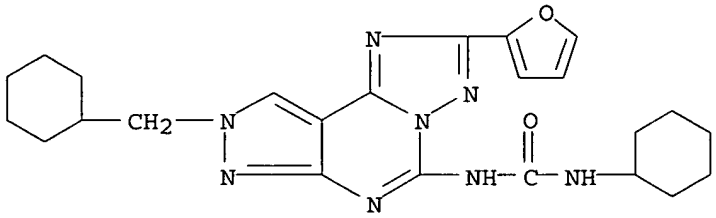
(9CI) (CA INDEX NAME)



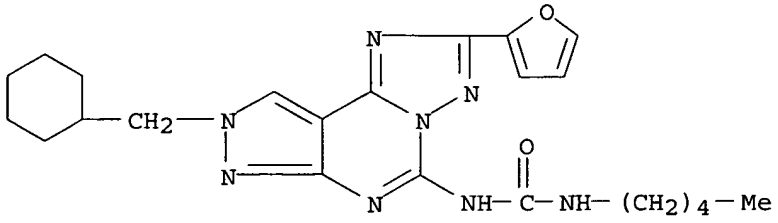
RN 827629-46-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



RN 827629-47-0 CAPLUS
CN Urea, N-cyclohexyl-N'-[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

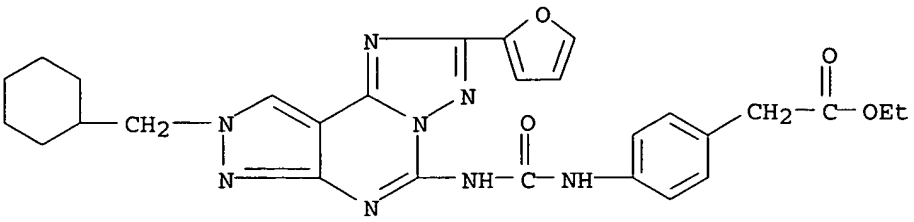


RN 827629-48-1 CAPLUS
CN Urea, N-[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-pentyl- (9CI) (CA INDEX NAME)

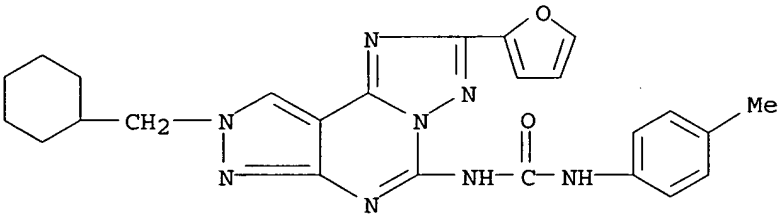


RN 827629-49-2 CAPLUS

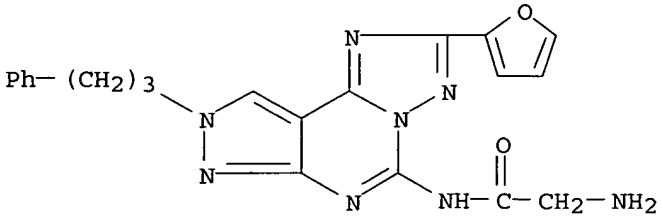
CN Benzeneacetic acid, 4-[[[[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



RN 827629-50-5 CAPLUS
CN Urea, N-[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



RN 852676-85-8 CAPLUS
CN Acetamide, 2-amino-N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1106821 CAPLUS
DOCUMENT NUMBER: 142:147845
TITLE: Combined Target-Based and Ligand-Based Drug Design Approach as a Tool To Define a Novel 3D-Pharmacophore

Model of Human A3 Adenosine Receptor Antagonists: Pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine Derivatives as a Key Study

AUTHOR(S): Moro, Stefano; Braiuca, Paolo; Deflorian, Francesca; Ferrari, Cristina; Pastorin, Giorgia; Cacciari, Barbara; Baraldi, Pier Giovanni; Varani, Katia; Borea, Pier Andrea; Spalluto, Giampiero

CORPORATE SOURCE: Molecular Modeling Section, Dipartimento di Scienze Farmaceutiche, Universita di Padova, Padua, I-35131, Italy

SOURCE: Journal of Medicinal Chemistry (2005), 48(1), 152-162
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

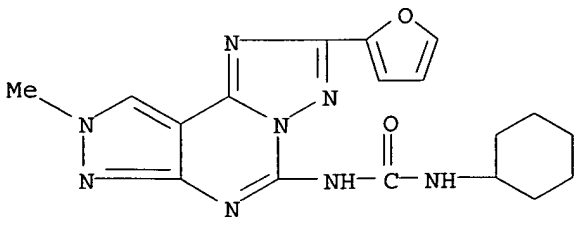
OTHER SOURCE(S): CASREACT 142:147845

AB A combined target-based and ligand-based drug design approach has been carried out to define a novel pharmacophore model of the human A3 receptor antagonists. High throughput mol. docking and comparative mol. field anal. (CoMFA) have been used in tandem to assemble a new target based pharmacophore model. In parallel, to provide more accurate information about the putative binding site of these A3 inhibitors, a rhodopsin-based model of the human A3 receptor was built and a novel Y-shape binding motif has been proposed. Docking-based structure superimposition has been used to perform a quant. study of the structure-activity relationships for binding of these pyrazolo-triazolo-pyrimidines to adenosine A3 receptor using CoMFA. Both steric and the electrostatic contour plots obtained from the CoMFA anal. nicely fit on the hypothetical binding site obtained by mol. docking. On the basis of the combined hypothesis, we have designed, synthesized, and tested 17 new derivs. Consistently, the predicted Ki values were very close to the exptl. values.

IT **827629-36-7P 827629-37-8P 827629-38-9P**
827629-39-0P 827629-40-3P 827629-41-4P
827629-42-5P 827629-43-6P 827629-44-7P
827629-45-8P 827629-46-9P 827629-47-0P
827629-48-1P 827629-49-2P 827629-50-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target- and ligand-based drug design approach to define novel 3D-pharmacophore model of A3 adenosine receptor antagonists: pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine derivs. as key study)

RN 827629-36-7 CAPLUS

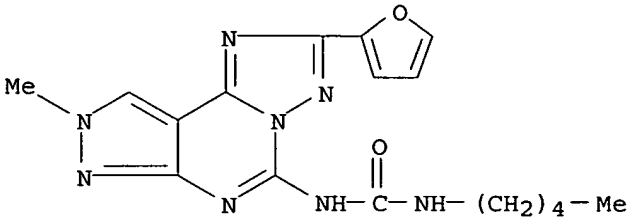
CN Urea, N-cyclohexyl-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



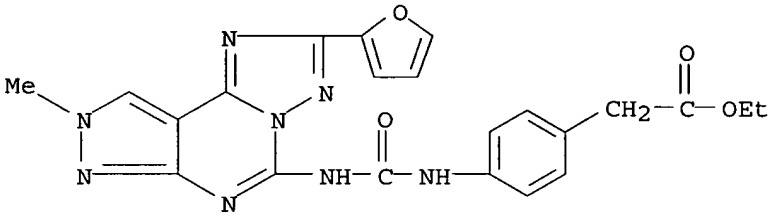
RN 827629-37-8 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-

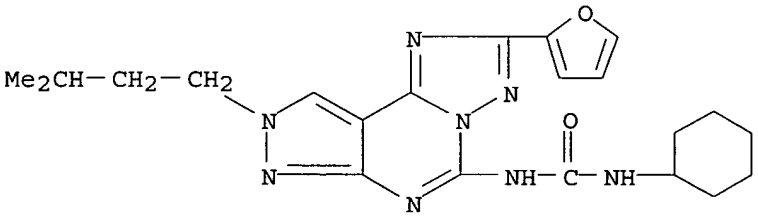
c]pyrimidin-5-yl]-N'-pentyl- (9CI) (CA INDEX NAME)



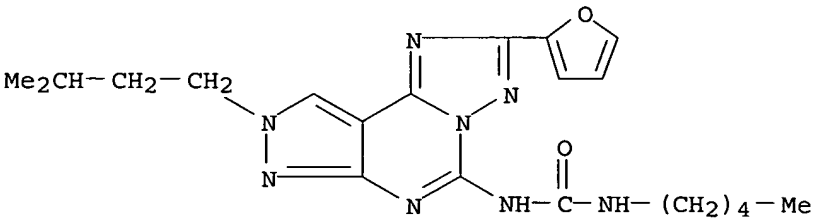
RN 827629-38-9 CAPLUS
CN Benzeneacetic acid, 4-[[[[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



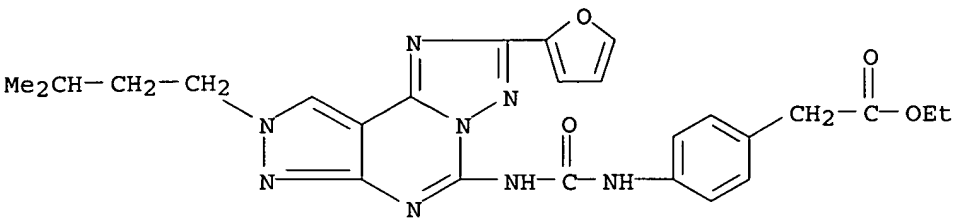
RN 827629-39-0 CAPLUS
CN Urea, N-cyclohexyl-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



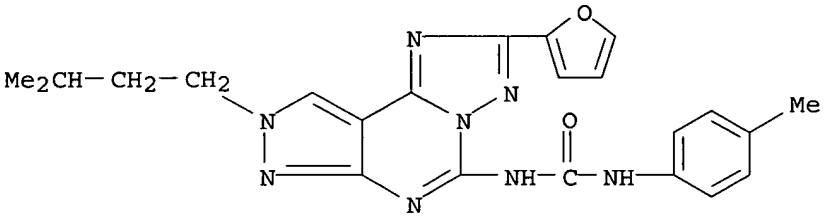
RN 827629-40-3 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-pentyl- (9CI) (CA INDEX NAME)



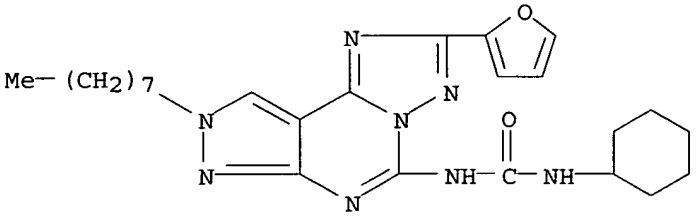
RN 827629-41-4 CAPLUS
CN Benzeneacetic acid, 4-[[[[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



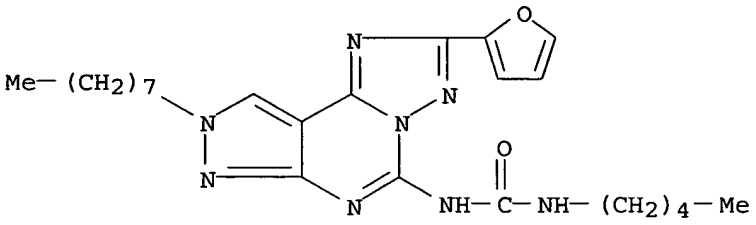
RN 827629-42-5 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



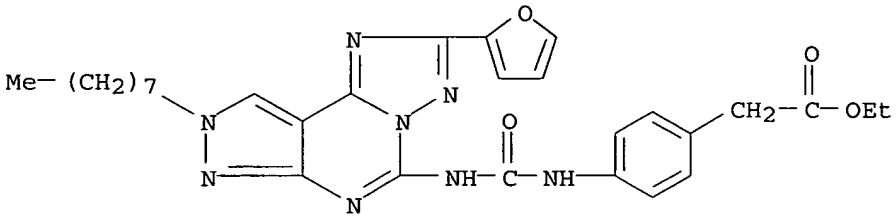
RN 827629-43-6 CAPLUS
CN Urea, N-cyclohexyl-N'-[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



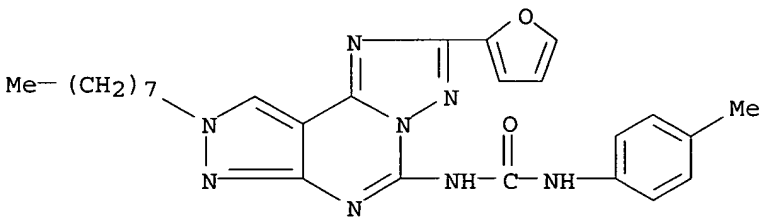
RN 827629-44-7 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-pentyl- (9CI) (CA INDEX NAME)



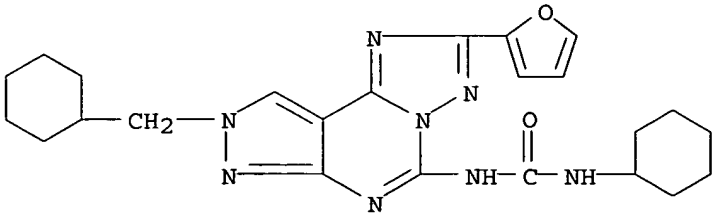
RN 827629-45-8 CAPLUS
CN Benzeneacetic acid, 4-[[[[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



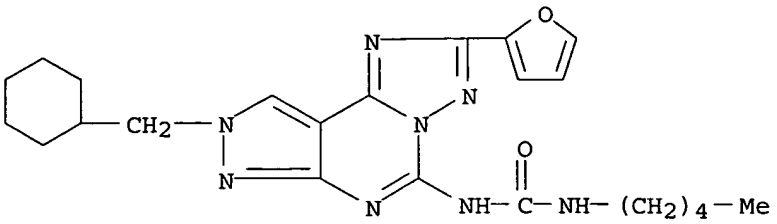
RN 827629-46-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-octyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



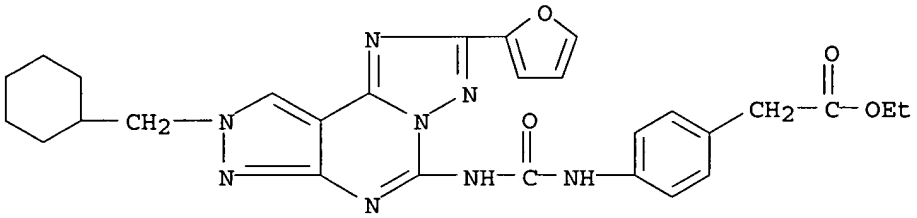
RN 827629-47-0 CAPLUS
CN Urea, N-cyclohexyl-N'-[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



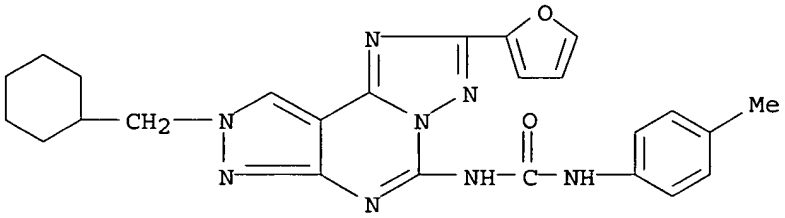
RN 827629-48-1 CAPLUS
CN Urea, N-[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-pentyl- (9CI) (CA INDEX NAME)



RN 827629-49-2 CAPLUS
CN Benzeneacetic acid, 4-[[[[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



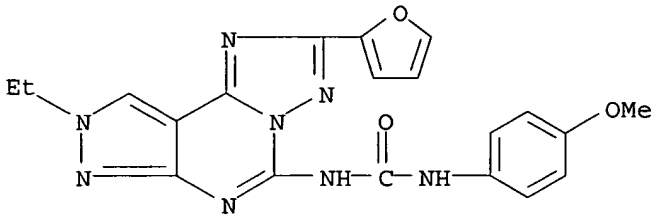
RN 827629-50-5 CAPLUS
CN Urea, N-[8-(cyclohexylmethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



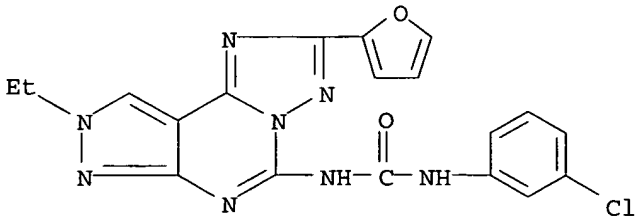
IT **252979-41-2 252979-42-3 252979-43-4**
252979-44-5 252979-45-6 252979-46-7
252979-47-8 252979-48-9 261629-22-5
261629-23-6 261629-24-7 261629-25-8
261629-26-9 261629-27-0 261629-28-1
261629-29-2 264623-54-3 321661-16-9
321661-18-1 321661-27-2 321661-29-4
321661-35-2 321661-36-3 321661-37-4
321661-38-5 361484-61-9 361484-62-0
361484-63-1 361484-64-2 385441-71-4
385441-72-5 385441-73-6 385441-74-7
385441-75-8 385441-76-9 385441-77-0
385441-78-1 385441-79-2 385441-80-5
385441-81-6 385441-82-7 385441-86-1
385441-87-2 396653-58-0 404011-36-5

404011-37-6 404011-38-7 404011-39-8
404011-40-1 404011-41-2 404011-42-3
404011-43-4 404011-44-5 404011-45-6
404011-46-7 404011-47-8 404011-48-9
404011-49-0 404011-50-3 404011-51-4
404011-52-5 404011-53-6 404011-54-7
404011-55-8 404011-56-9 404011-57-0
404011-58-1 404011-59-2 404011-60-5
404011-61-6 404011-62-7 404011-63-8
404011-64-9 404011-65-0 404011-66-1
404011-67-2 404011-68-3 404011-69-4
404011-70-7 404011-71-8 404011-72-9
404011-73-0 404011-74-1 404011-75-2
404011-76-3 404011-77-4 404011-78-5
404011-79-6 404011-80-9 404011-81-0
404011-82-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(target- and ligand-based drug design approach to define novel 3D-pharmacophore model of A3 adenosine receptor antagonists: pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine derivs. as key study)

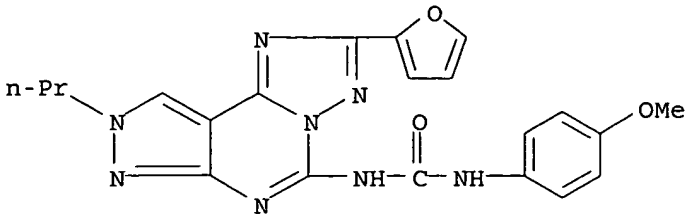
RN 252979-41-2 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



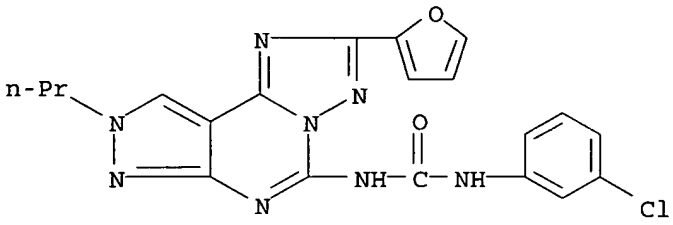
RN 252979-42-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



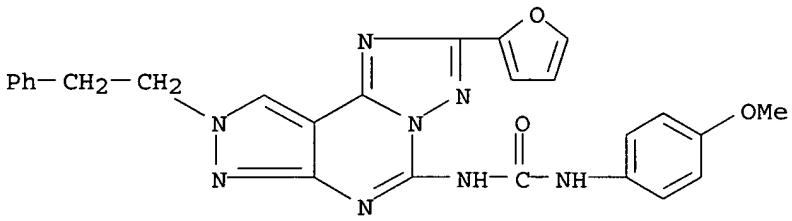
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



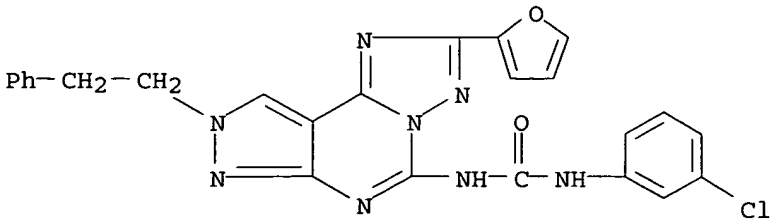
RN 252979-44-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 252979-45-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

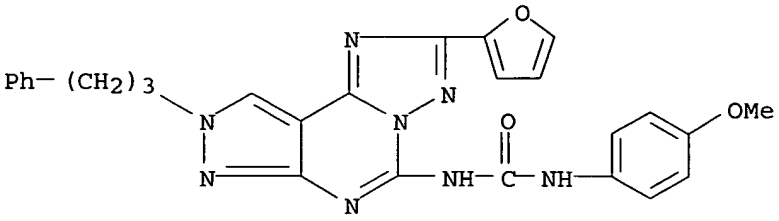


RN 252979-46-7 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

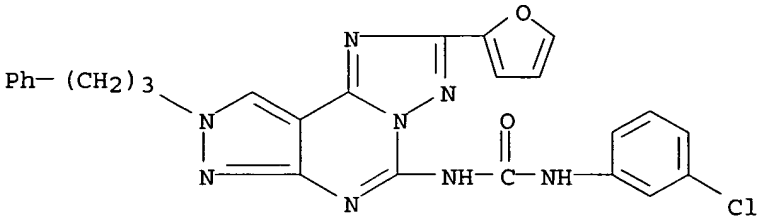


RN 252979-47-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-

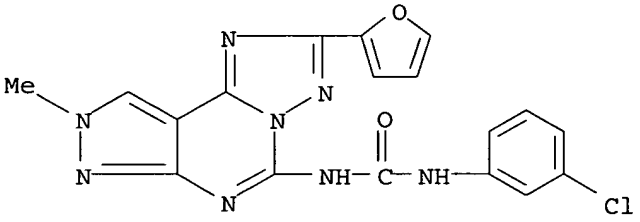
e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



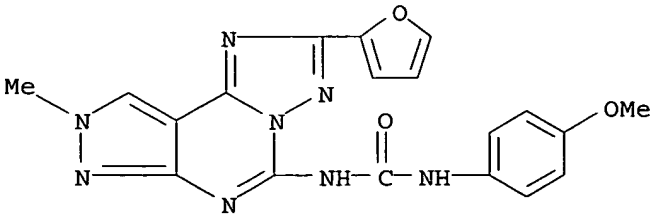
RN 252979-48-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



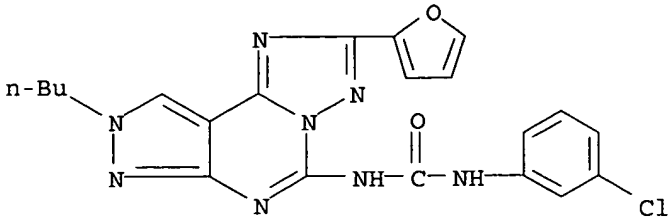
RN 261629-22-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



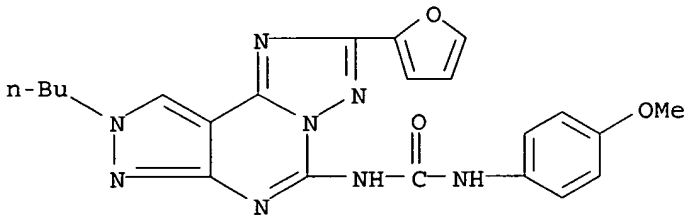
RN 261629-23-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



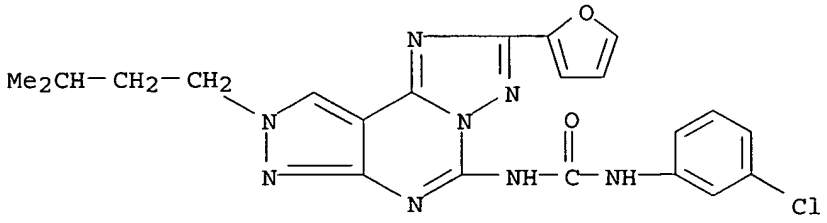
RN 261629-24-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



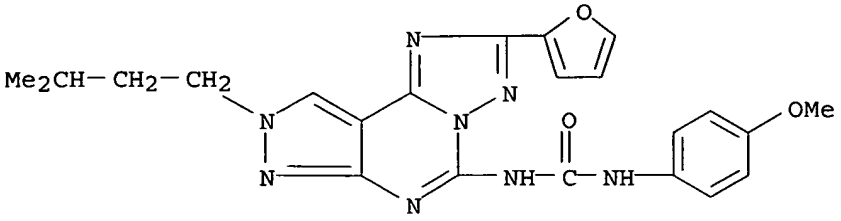
RN 261629-25-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



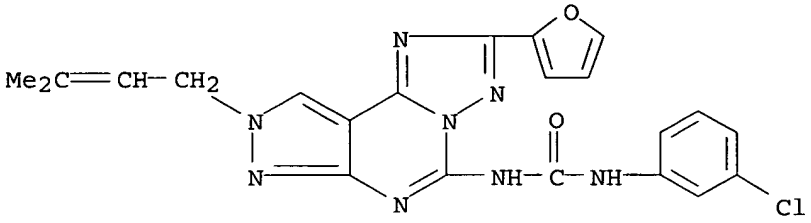
RN 261629-26-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



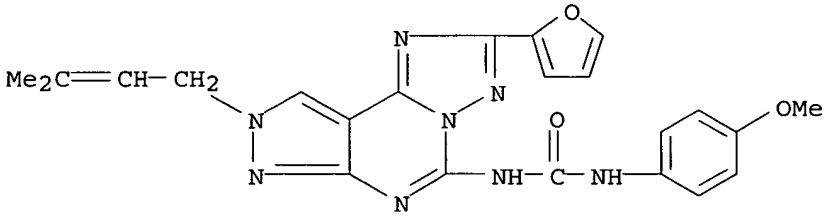
RN 261629-27-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



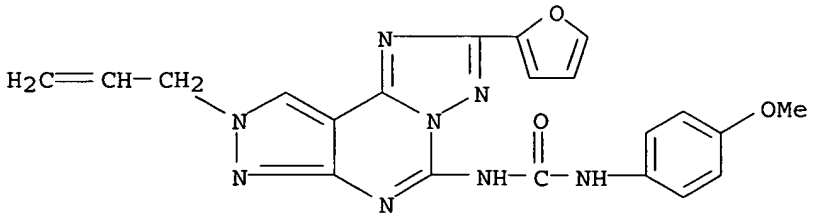
RN 261629-28-1 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 261629-29-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

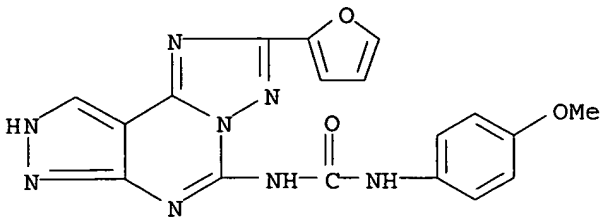


RN 264623-54-3 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-propenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

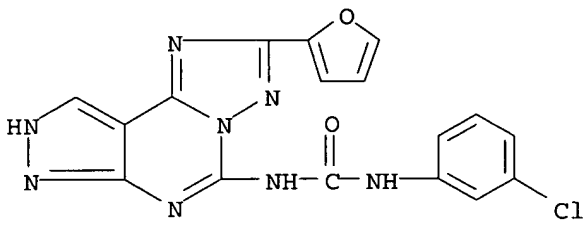


RN 321661-16-9 CAPLUS

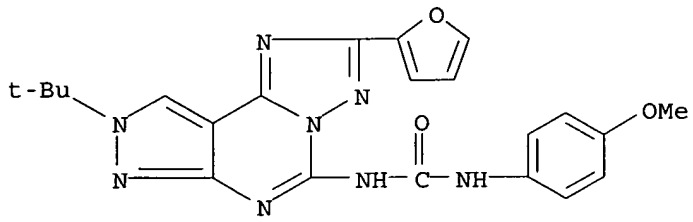
CN Urea, N-[2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



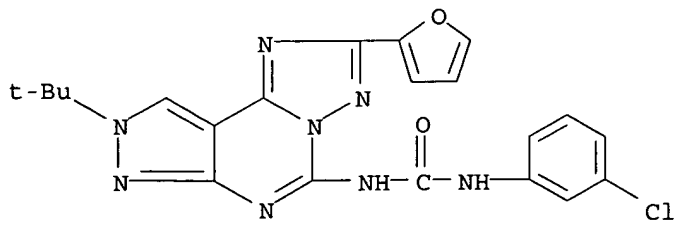
RN 321661-18-1 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



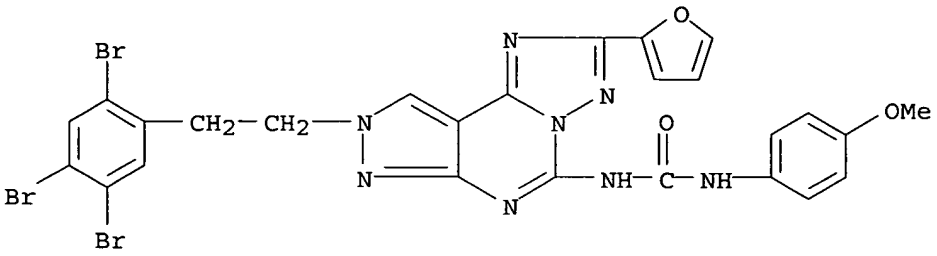
RN 321661-27-2 CAPLUS
CN Urea, N-[8-(1,1-dimethylethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



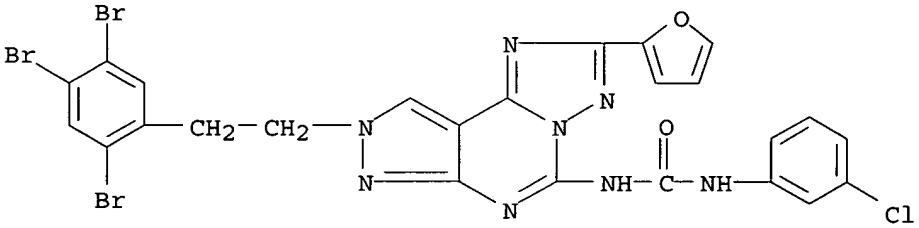
RN 321661-29-4 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-(1,1-dimethylethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 321661-35-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-[2-(2,4,5-tribromophenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

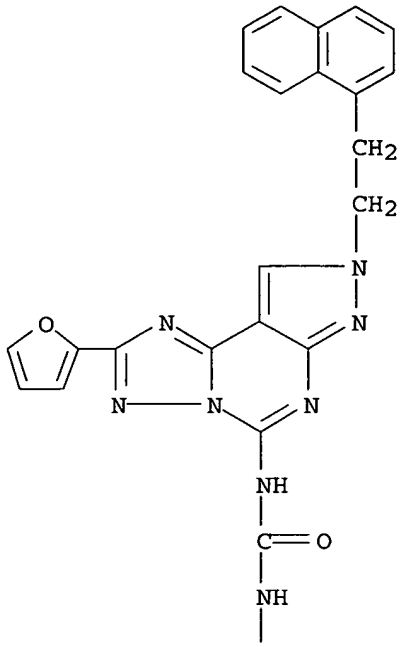


RN 321661-36-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-[2-(2,4,5-tribromophenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

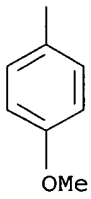


RN 321661-37-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-[2-(1-naphthalenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

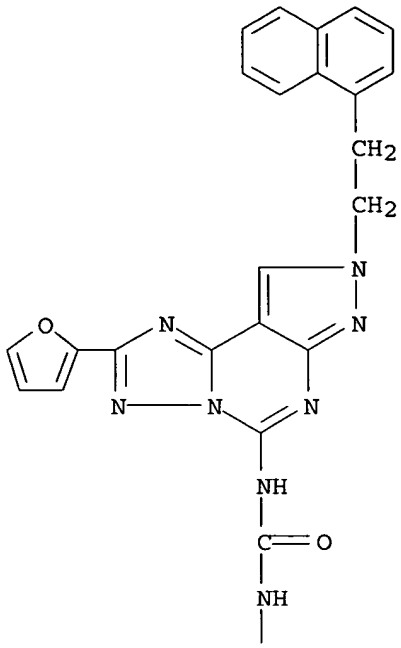


PAGE 2-A

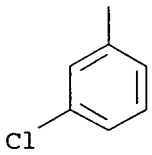


RN 321661-38-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-[2-(1-naphthalenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

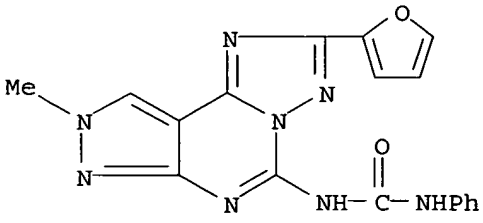
PAGE 1-A



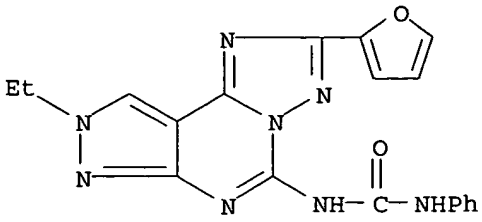
PAGE 2-A



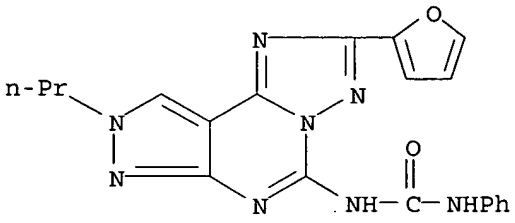
RN 361484-61-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



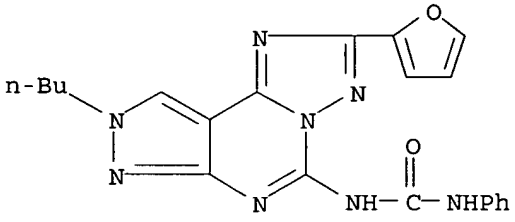
RN 361484-62-0 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



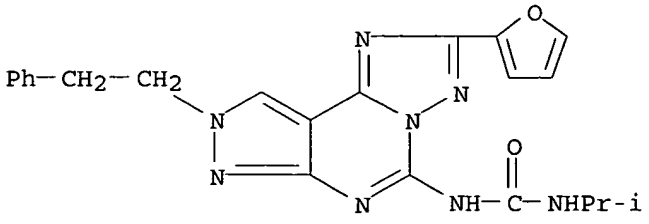
RN 361484-63-1 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



RN 361484-64-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)

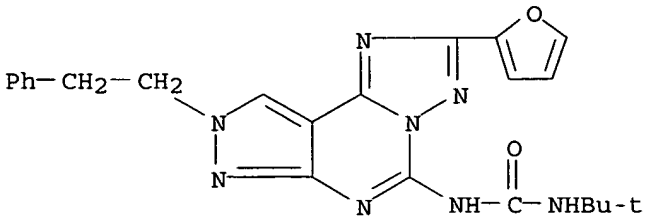


RN 385441-71-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

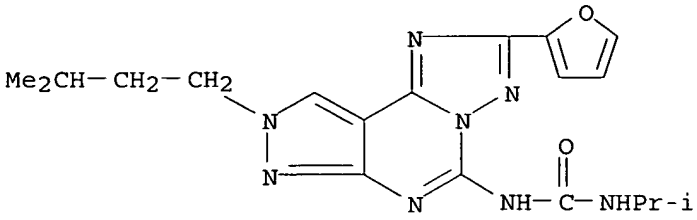


RN 385441-72-5 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX

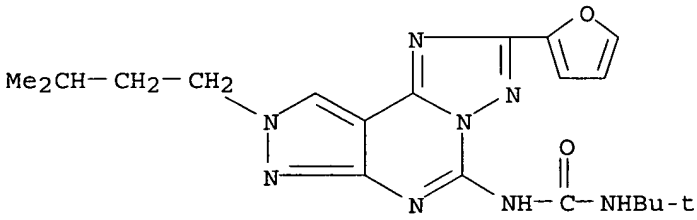
NAME)



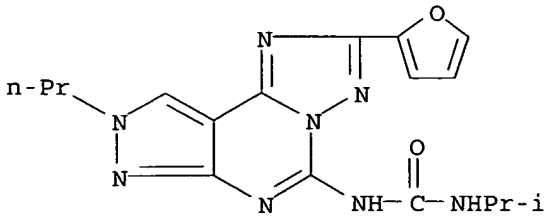
RN 385441-73-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



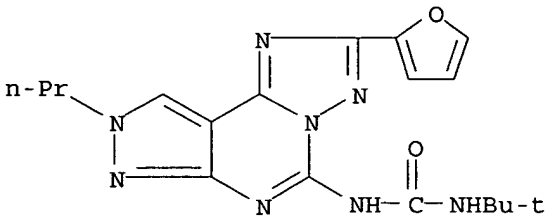
RN 385441-74-7 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



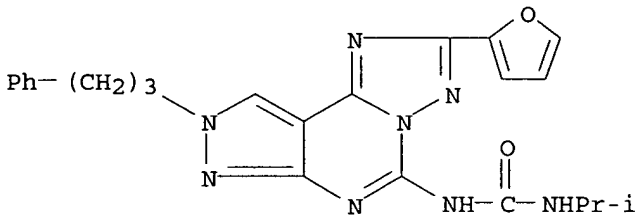
RN 385441-75-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



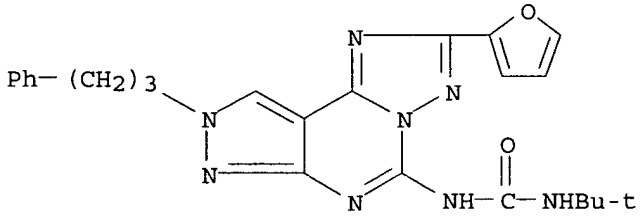
RN 385441-76-9 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



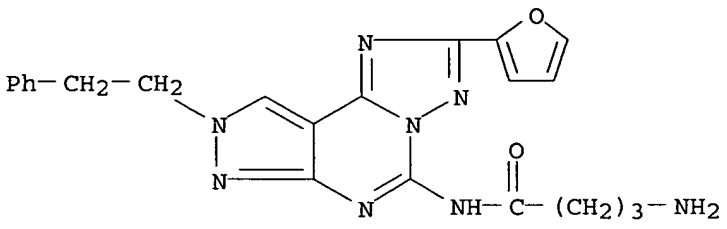
RN 385441-77-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 385441-78-1 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

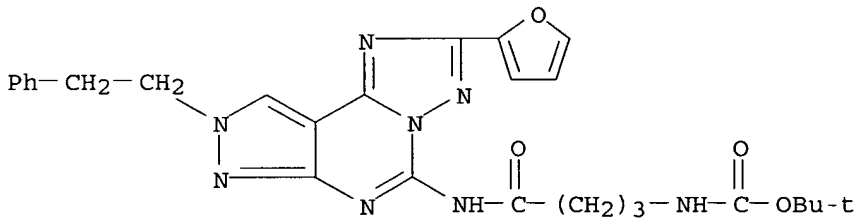


RN 385441-79-2 CAPLUS
CN Butanamide, 4-amino-N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

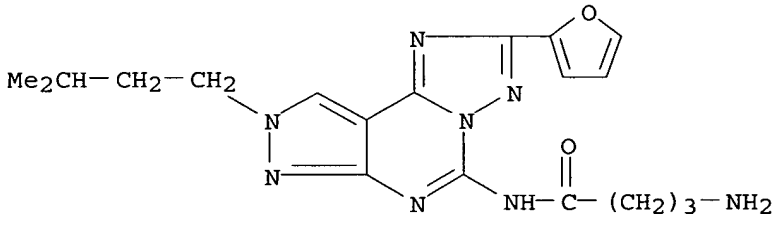


● HCl

RN 385441-80-5 CAPLUS
CN Carbamic acid, [4-[[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]-4-oxobutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

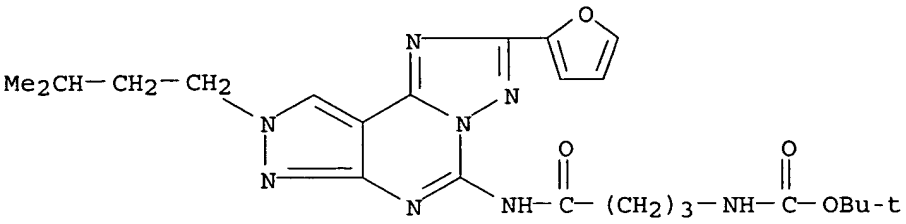


RN 385441-81-6 CAPLUS
CN Butanamide, 4-amino-N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

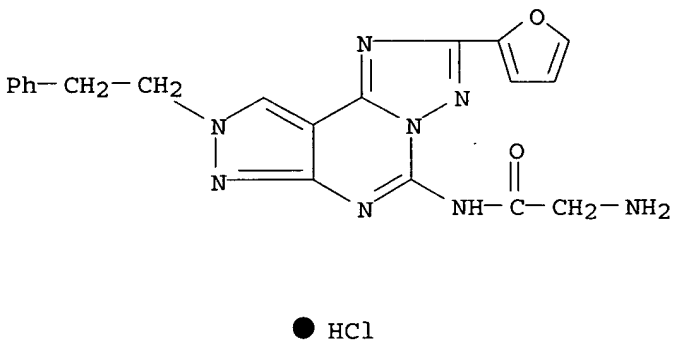


● HCl

RN 385441-82-7 CAPLUS
CN Carbamic acid, [4-[[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]-4-oxobutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

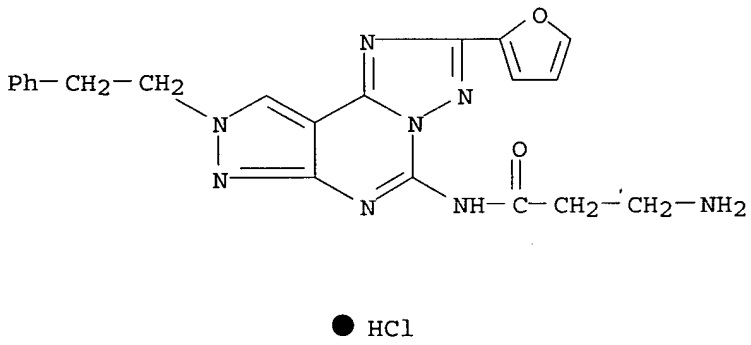


RN 385441-86-1 CAPLUS
CN Acetamide, 2-amino-N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



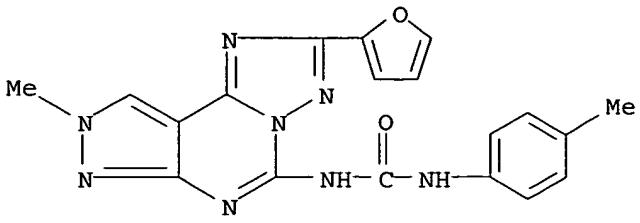
● HCl

RN 385441-87-2 CAPLUS
CN Propanamide, 3-amino-N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

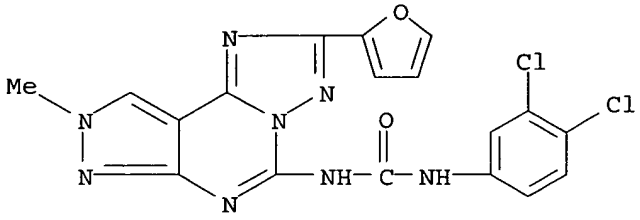


● HCl

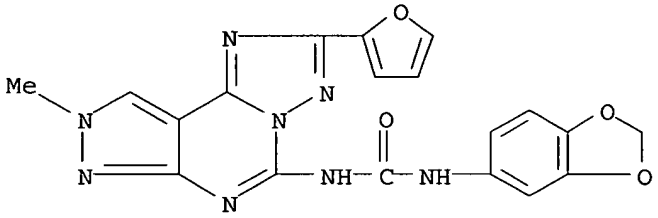
RN 396653-58-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



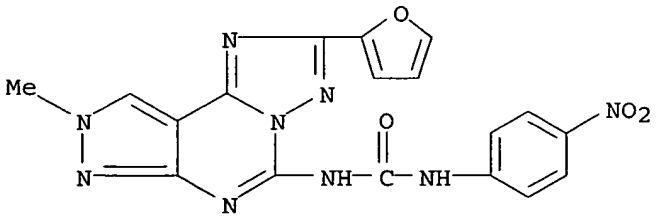
RN 404011-36-5 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



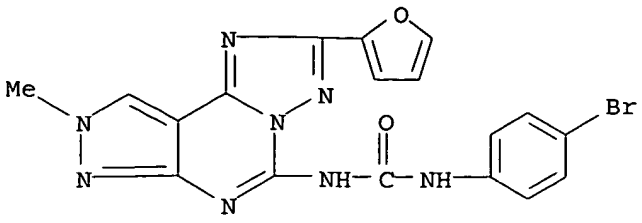
RN 404011-37-6 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



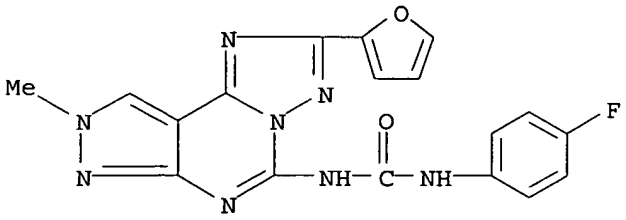
RN 404011-38-7 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



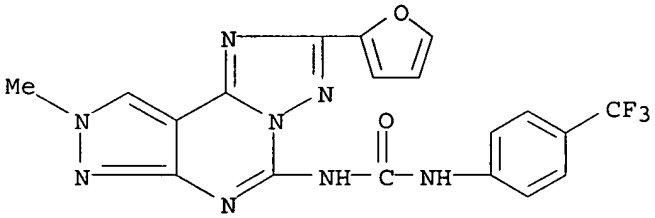
RN 404011-39-8 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



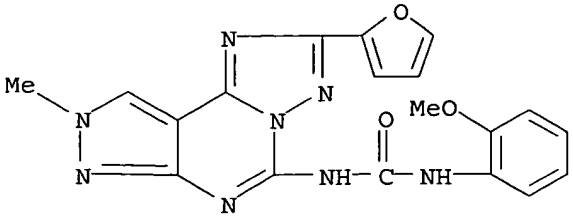
RN 404011-40-1 CAPLUS
CN Urea, N-(4-fluorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



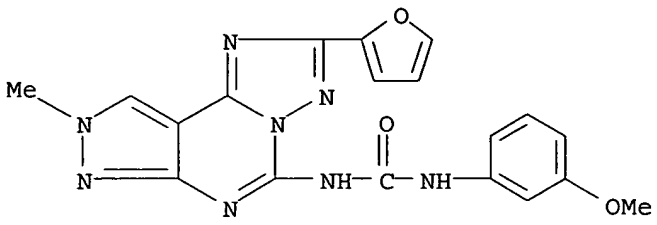
RN 404011-41-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



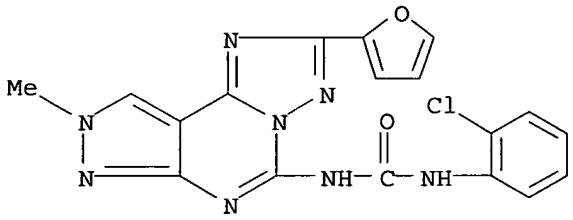
RN 404011-42-3 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



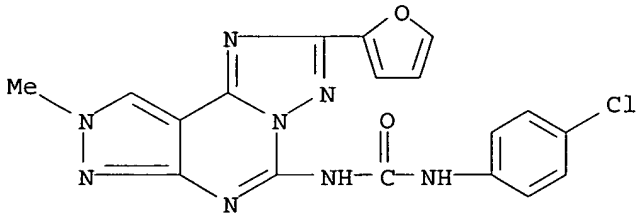
RN 404011-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



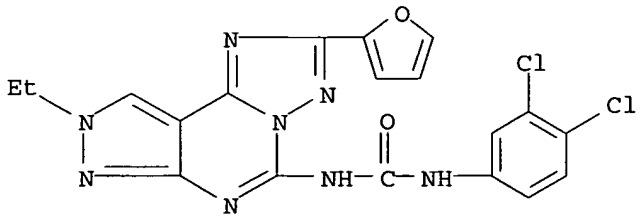
RN 404011-44-5 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 404011-45-6 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

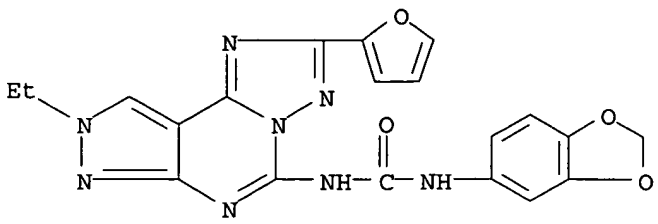


RN 404011-46-7 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

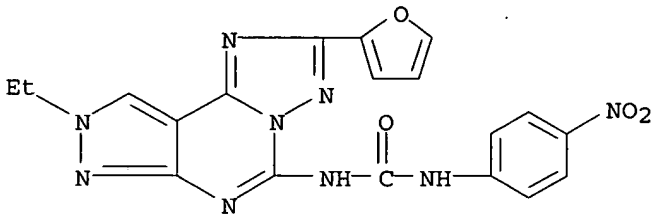


RN 404011-47-8 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-

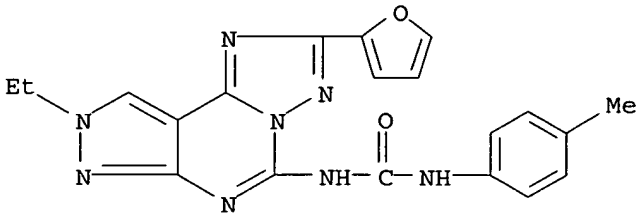
e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



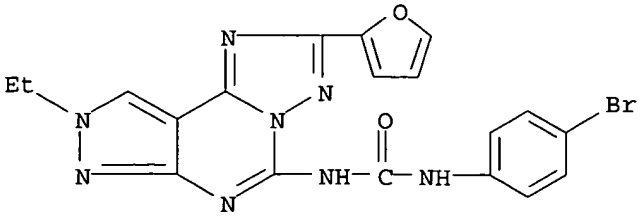
RN 404011-48-9 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



RN 404011-49-0 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)

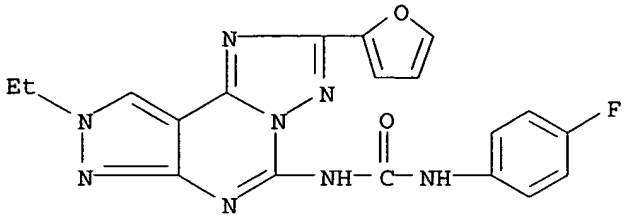


RN 404011-50-3 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

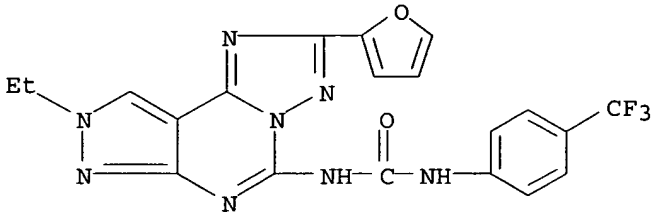


RN 404011-51-4 CAPLUS

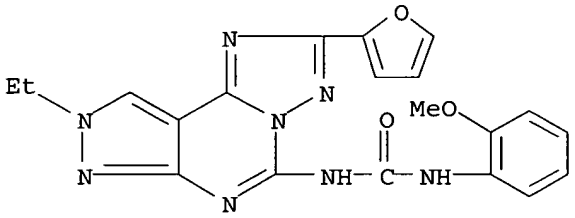
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



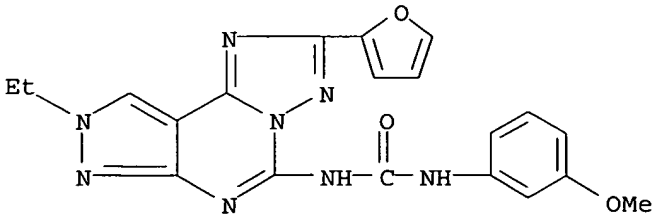
RN 404011-52-5 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



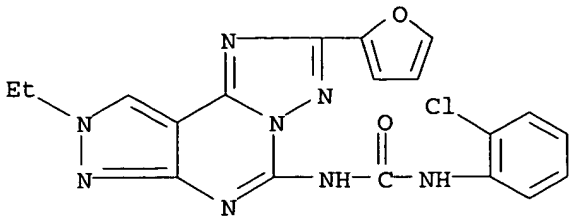
RN 404011-53-6 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



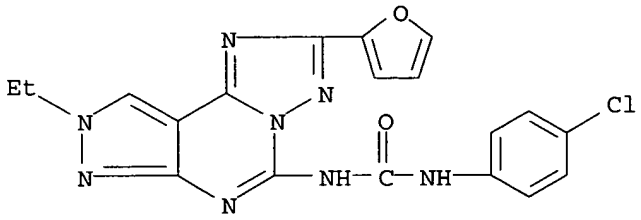
RN 404011-54-7 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



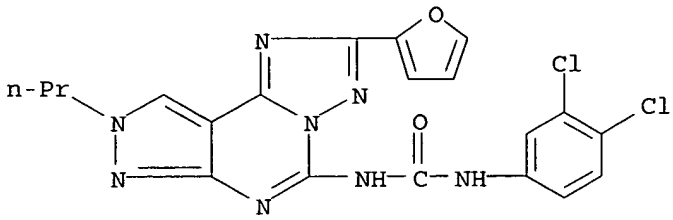
RN 404011-55-8 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



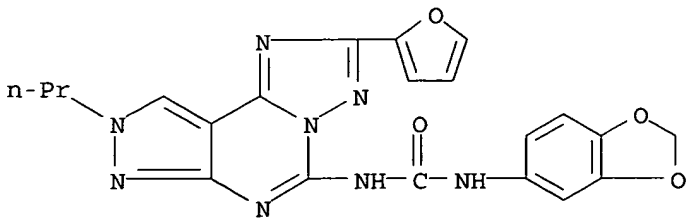
RN 404011-56-9 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



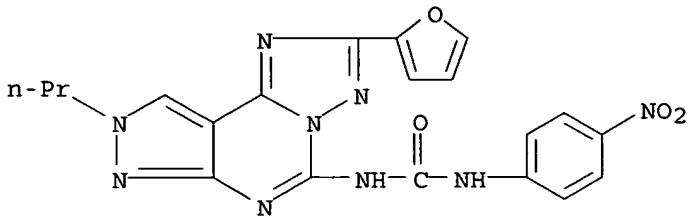
RN 404011-57-0 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



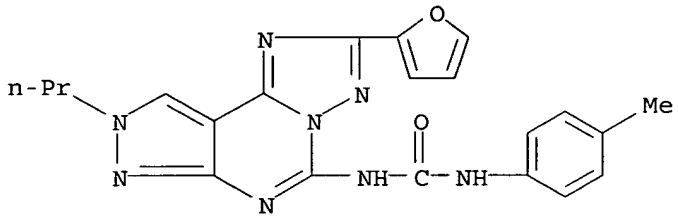
RN 404011-58-1 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



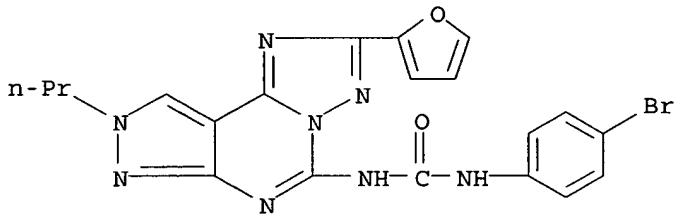
RN 404011-59-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



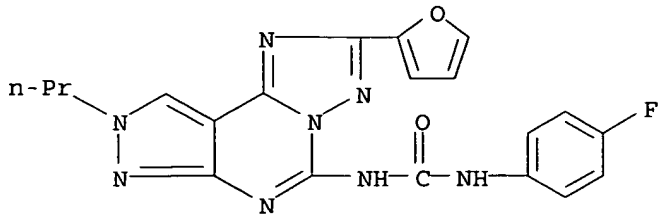
RN 404011-60-5 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



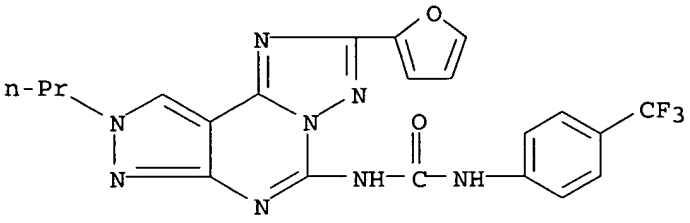
RN 404011-61-6 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



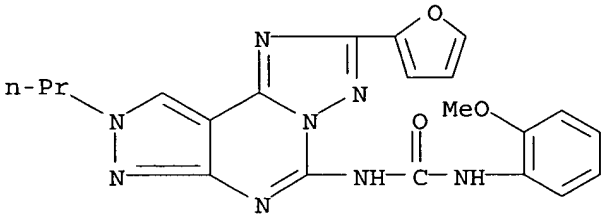
RN 404011-62-7 CAPLUS
CN Urea, N-(4-fluorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



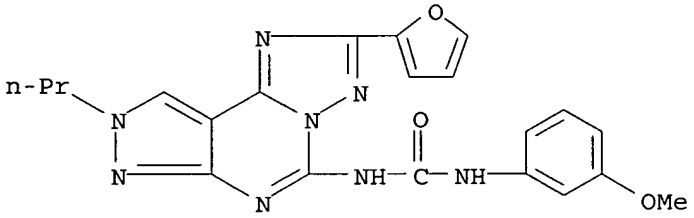
RN 404011-63-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



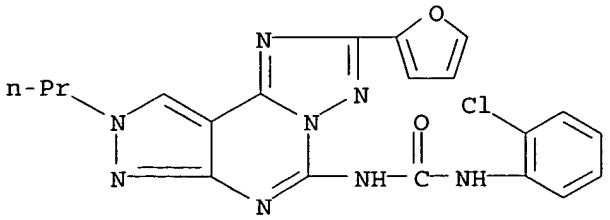
RN 404011-64-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



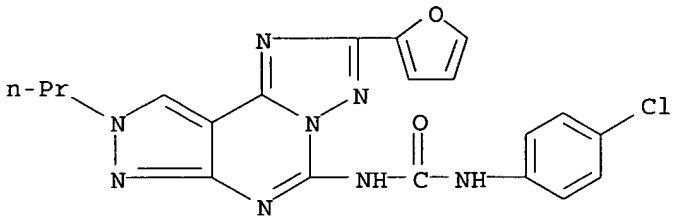
RN 404011-65-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



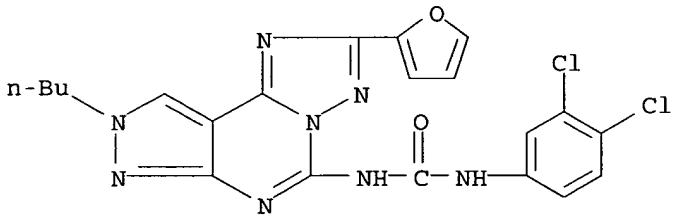
RN 404011-66-1 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



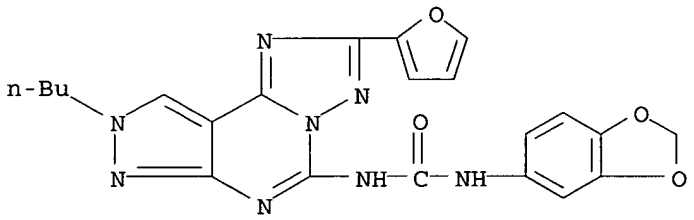
RN 404011-67-2 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



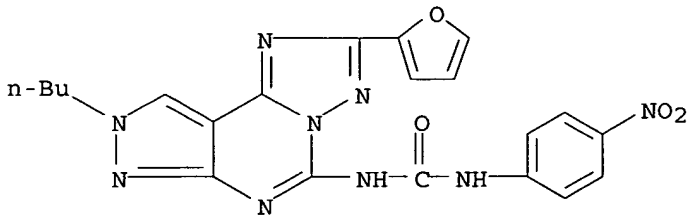
RN 404011-68-3 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



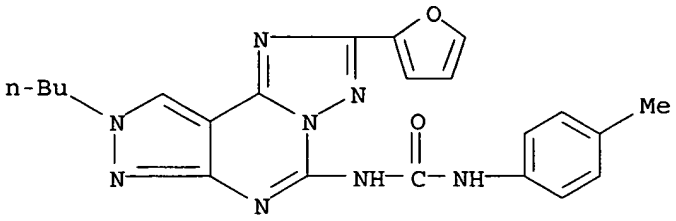
RN 404011-69-4 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



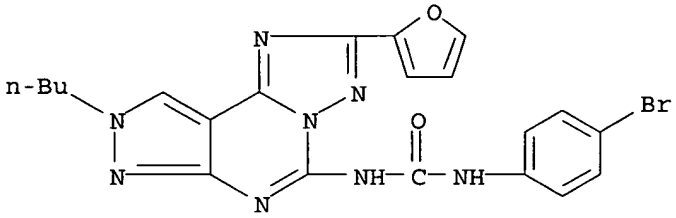
RN 404011-70-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



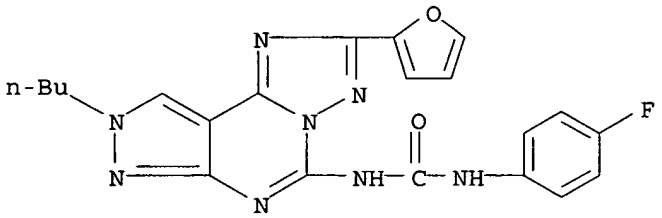
RN 404011-71-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



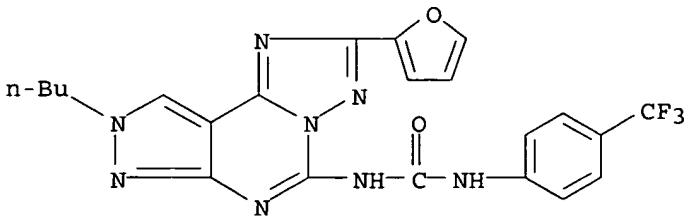
RN 404011-72-9 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



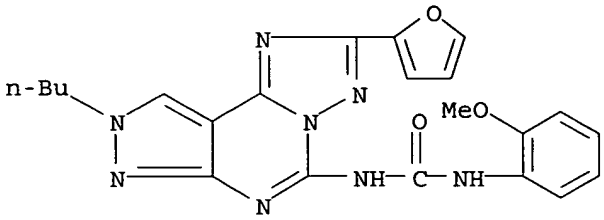
RN 404011-73-0 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



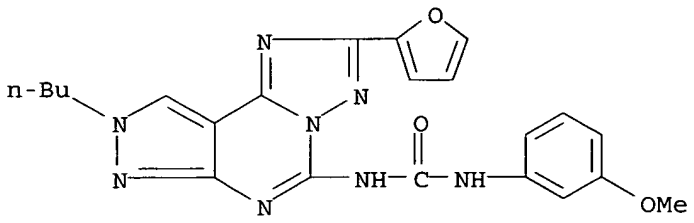
RN 404011-74-1 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



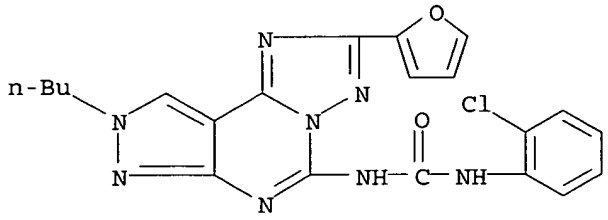
RN 404011-75-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



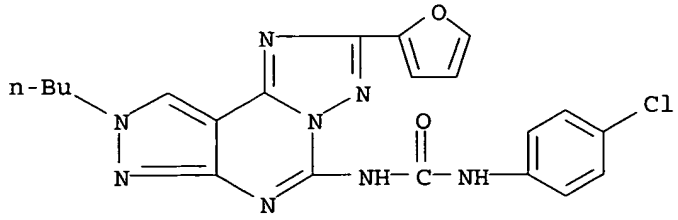
RN 404011-76-3 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



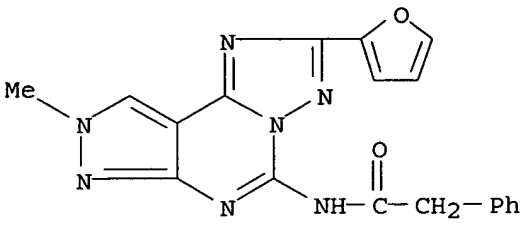
RN 404011-77-4 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-chlorophenyl)- (9CI) (CA INDEX NAME)



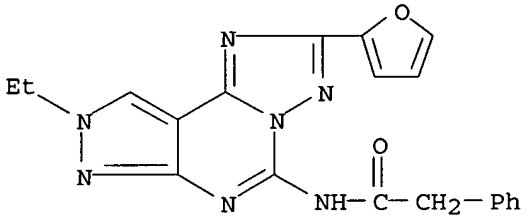
RN 404011-78-5 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



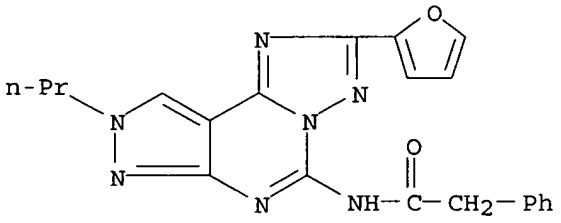
RN 404011-79-6 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



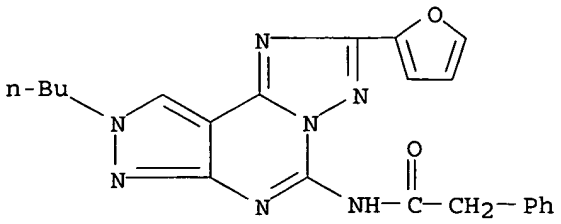
RN 404011-80-9 CAPLUS
CN Benzeneacetamide, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 404011-81-0 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 404011-82-1 CAPLUS
CN Benzeneacetamide, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



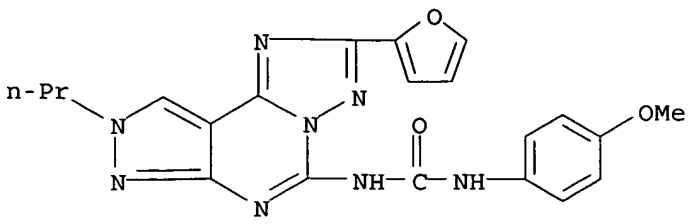
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:166375 CAPLUS
DOCUMENT NUMBER: 140:281756
TITLE: Expression of A3 adenosine receptors in human lymphocytes: Up-regulation in T cell activation
AUTHOR(S): Gessi, Stefania; Varani, Katia; Merighi, Stefania; Cattabriga, Elena; Avitabile, Arianna; Gavioli, Riccardo; Fortini, Cinzia; Leung, Edward; Mac Lennan, Stephen; Borea, Pier Andrea
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Ferrara, Italy
SOURCE: Molecular Pharmacology (2004), 65(3), 711-719
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study investigates mRNA and protein levels of A3 adenosine receptors in resting (R) and activated (A) human lymphocytes. The receptors were evaluated by the antagonist radioligand [3H]5-N-(4-methoxyphenyl-carbamoyl)amino-8-propyl-2(2furyl)-pyrazolo-[4,3e]-1,2,4-triazolo-[1,5-c]-pyrimidine ([3H]MRE 3008F20), which yielded Bmax values of 125 and 225 fmol/mg of protein and KD values of 1.79 and 1.85 nM in R and A cells, resp. The protein seems to be induced with remarkable rapidity starting at 15 min and reaches a plateau at 30 min. Western blot assays revealed that the up-regulation of the A3 subtype after lymphocyte activation was caused by an increase in an enriched CD4- cell fraction. Real-time reverse transcription-polymerase chain reaction expts. confirmed the rapid increase of A3 mRNA after T cell activation. Competition of radioligand binding by adenosine ligands displayed a rank order of potency typical of the A3 subtype. Thermodn. data indicated that the binding is enthalpy- and entropy-driven in both R and A cells, suggesting that the activation process does not involve, at a mol. level, receptor alterations leading to modifications in the A3-related binding mechanisms. Functionally, the up-regulation of A3 adenosine receptors in A vs. R cells corresponded to a potency increase of the A3 agonist N6-(3-iodo-benzyl)-2-chloro-adenosine-5'-N-methyluronamide in inhibiting cAMP accumulation (IC50 = 1.5 and 2.7 nM, resp.); this effect was antagonized by MRE 3008F20 (IC50 = 5.0 nM). In conclusion, the authors' results provide, for the first time, an in-depth investigation of A3 receptors in human lymphocytes and demonstrate that, under activating conditions, they are up-regulated and may contribute to the effects triggered by adenosine.

IT **252979-43-4**, MRE 3008F20
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PKT (Pharmacokinetics); PYP (Physical process); BIOL (Biological study); PROC (Process)
(A3 adenosine receptors expression and characterization in human lymphocytes and up-regulation in T cell activation)

RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:2642 CAPLUS
DOCUMENT NUMBER: 140:70996
TITLE: Enhancing treatment of MDR cancer with adenosine A3 antagonists
INVENTOR(S): Borea, Pier Andrea; Baraldi, Pier Giovanni; Chen, Shih-Fong; Leung, Edward
PATENT ASSIGNEE(S): King Pharmaceuticals Research & Development, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000237	A2	20031231	WO 2003-US20118	20030624
WO 2004000237	A3	20040226		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2464539	AA	20031231	CA 2003-2464539	20030624
AU 2003245693	A1	20040106	AU 2003-245693	20030624
US 2004067932	A1	20040408	US 2003-603406	20030624
BR 2003005106	A	20040928	BR 2003-5106	20030624
EP 1515719	A2	20050323	EP 2003-739312	20030624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005530858	T2	20051013	JP 2004-530977	20030624

PRIORITY APPLN. INFO.:

US 2002-391009P	P	20020624
US 2002-394395P	P	20020708
WO 2003-US20118	W	20030624

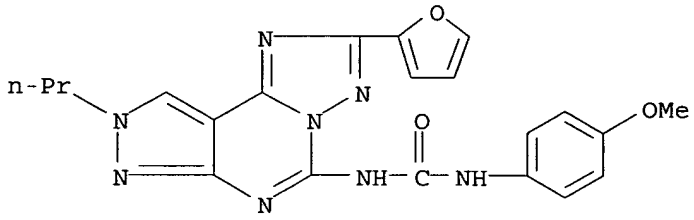
OTHER SOURCE(S): MARPAT 140:70996

AB The invention discloses the use of high affinity adenosine A3 receptor antagonists for enhancing chemotherapeutic treatment of cancers expressing adenosine A3 receptors and cancers expressing P-glycoprotein or MRP. In preferred embodiments, adenosine A3 receptor antagonists are administered before or during administration of a taxane family, vinca alkaloid,

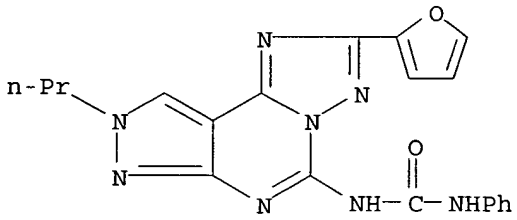
camptothecin or antibiotic chemotherapeutic agent.

IT **252979-43-4 361484-63-1 361484-64-2**
396653-58-0, MRE 3046F20 **638195-73-0 638195-74-1**
638195-75-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A3 antagonists for enhancing treatment of MDR cancer)

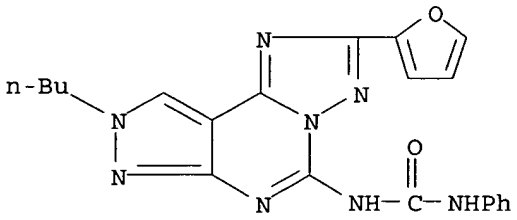
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



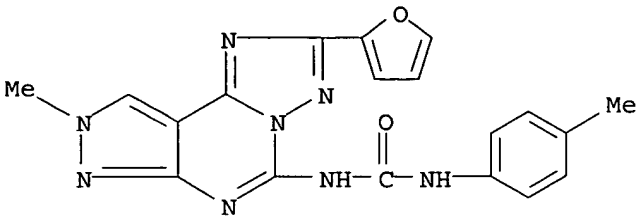
RN 361484-63-1 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



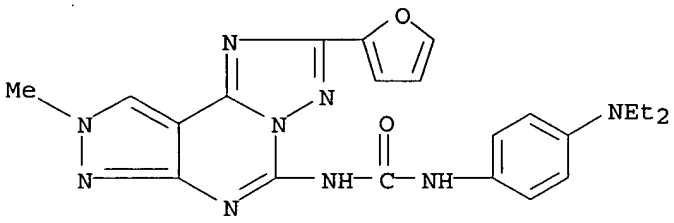
RN 361484-64-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



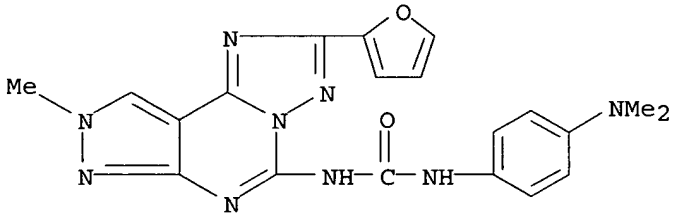
RN 396653-58-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



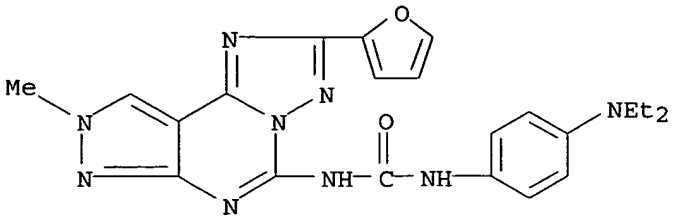
RN 638195-73-0 CAPLUS
CN Urea, N-[4-(diethylamino)phenyl]-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 638195-74-1 CAPLUS
CN Urea, N-[4-(dimethylamino)phenyl]-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 638195-75-2 CAPLUS
CN Urea, N-[4-(diethylamino)phenyl]-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L6 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:2631 CAPLUS
DOCUMENT NUMBER: 140:70994
TITLE: Enhancing treatment of MDR cancer with adenosine A3 antagonists
INVENTOR(S): Borea, Pier Andrea; Baraldi, Pier Giovanni; Chen, Shih-Fong; Leung, Edward
PATENT ASSIGNEE(S): King Pharmaceuticals Research & Development, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004000224	A2	20031231	WO 2003-US19687		20030620
WO 2004000224	A3	20040408			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003251595	A1	20040106	AU 2003-251595		20030620
US 2005119289	A1	20050602	US 2003-600116		20030620
ZA 2004001450	A	20050310	ZA 2004-1450		20040224
PRIORITY APPLN. INFO.:			US 2002-391009P	P	20020624
			WO 2003-US19687	W	20030620

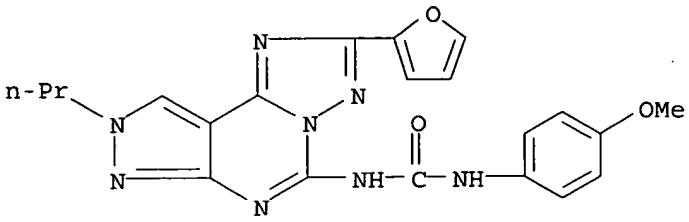
OTHER SOURCE(S): MARPAT 140:70994

AB The invention discloses the use of high affinity adenosine A3 receptor antagonists for enhancing chemotherapeutic treatment of cancers expressing adenosine A3 receptors and cancers expressing P-glycoprotein or MRP. In preferred embodiments, adenosine A3 receptor antagonists are administered before or during administration of a taxane family, vinca alkaloid, camptothecin or antibiotic chemotherapeutic agent.

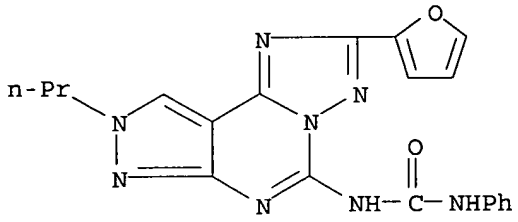
IT **252979-43-4 361484-63-1 361484-64-2 396653-58-0 638195-73-0 638195-74-1 638195-75-2**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A3 antagonists for enhancing treatment of MDR cancer)

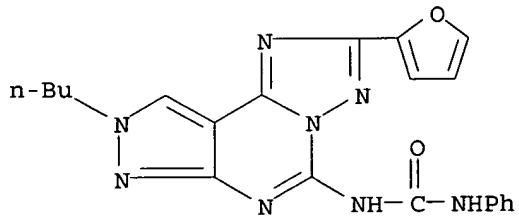
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



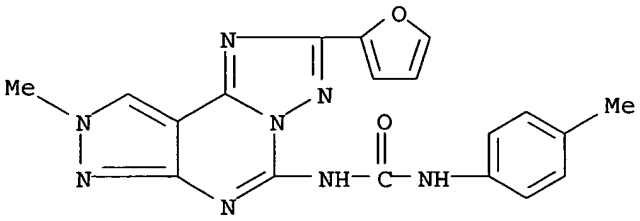
RN 361484-63-1 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



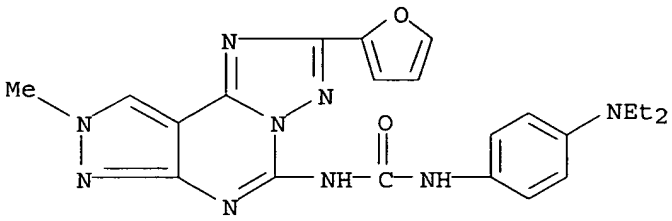
RN 361484-64-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



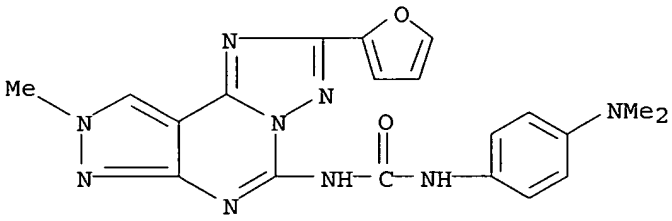
RN 396653-58-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



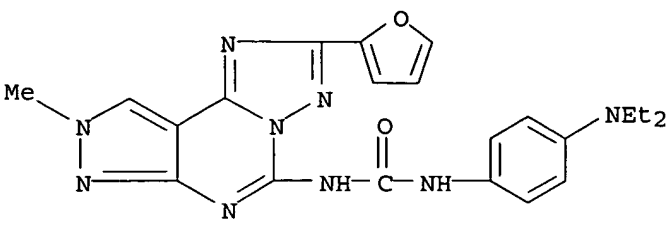
RN 638195-73-0 CAPLUS
CN Urea, N-[4-(diethylamino)phenyl]-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 638195-74-1 CAPLUS
CN Urea, N-[4-(dimethylamino)phenyl]-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 638195-75-2 CAPLUS
CN Urea, N-[4-(diethylamino)phenyl]-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L6 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:971891 CAPLUS
DOCUMENT NUMBER: 140:13098
TITLE: Pharmaceutically active compounds having a tricyclic pyrazolotriazolopyrimidine ring structure and methods of use
INVENTOR(S): Baraldi, Pier Giovanni; Borea, Pier Andrea
PATENT ASSIGNEE(S): King Pharmaceuticals Research & Development, Inc., USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101455	A2	20031211	WO 2003-US17313	20030530
WO 2003101455	A3	20040521		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2454654	AA	20031211	CA 2003-2454654	20030530
AU 2003245380	A1	20031219	AU 2003-245380	20030530
US 2004039004	A1	20040226	US 2003-452788	20030530
BR 2003004963	A	20040928	BR 2003-4963	20030530
EP 1549319	A2	20050706	EP 2003-739019	20030530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005527635	T2	20050915	JP 2004-508812	20030530
ZA 2004000784	A	20050503	ZA 2004-784	20040130
PRIORITY APPLN. INFO.:			US 2002-384809P P	20020530
			WO 2003-US17313 W	20030530

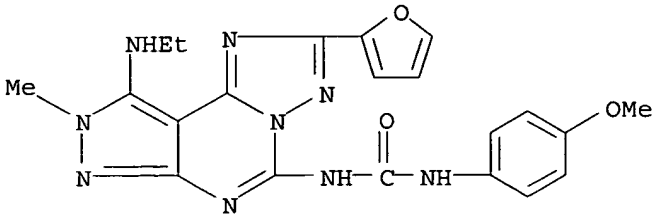
OTHER SOURCE(S): MARPAT 140:13098
AB Tricyclic pyrazolotriazolopyrimidines which possess antagonistic activity for adenosine receptors may be useful for modulating biol. function in the nervous, cardiovascular, renal, respiratory and immune systems. General

synthetic schemes and examples of formulations for the compds. are presented.

IT **512846-16-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(tricyclic pyrazolotriazolopyrimidines with antagonistic activity for adenosine receptors)

RN 512846-16-1 CAPLUS

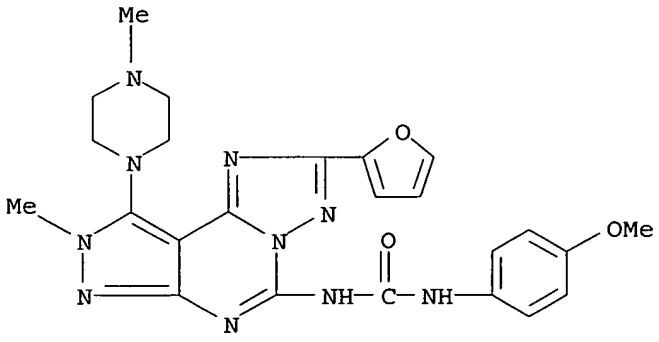
CN Urea, N-[9-(ethylamino)-2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



IT **512846-18-3P 512846-20-7P 512846-24-1P**
512846-26-3P 512846-28-5P 512846-38-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tricyclic pyrazolotriazolopyrimidines with antagonistic activity for adenosine receptors)

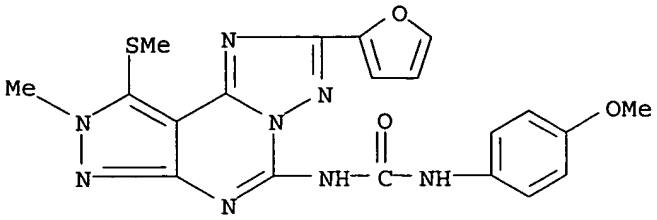
RN 512846-18-3 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-methyl-9-(4-methyl-1-piperazinyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

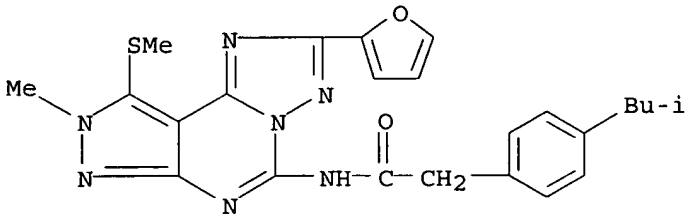


RN 512846-20-7 CAPLUS

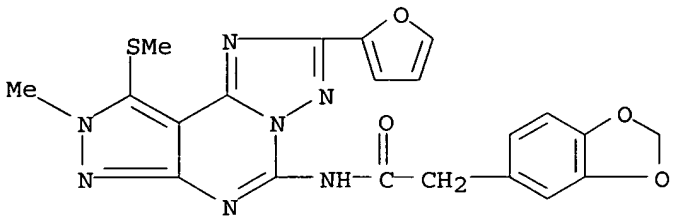
CN Urea, N-[2-(2-furanyl)-8-methyl-9-(methylthio)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



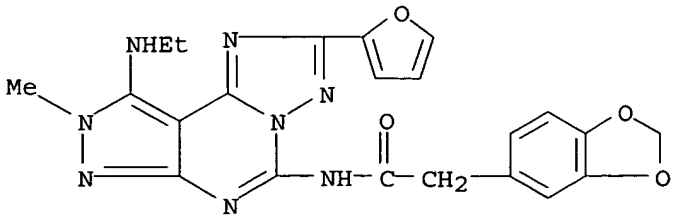
RN 512846-24-1 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-methyl-9-(methylthio)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 512846-26-3 CAPLUS
CN 1,3-Benzodioxole-5-acetamide, N-[2-(2-furanyl)-8-methyl-9-(methylthio)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

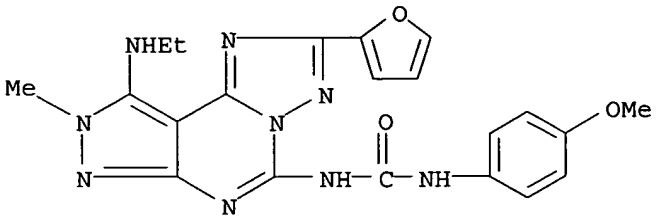


RN 512846-28-5 CAPLUS
CN 1,3-Benzodioxole-5-acetamide, N-[9-(ethylamino)-2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



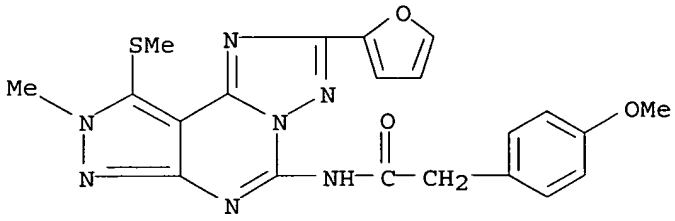
RN 512846-38-7 CAPLUS

CN Urea, N-[9-(ethylamino)-2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **512846-22-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tricyclic pyrazolotriazolopyrimidines with antagonistic activity for adenosine receptors)
RN 512846-22-9 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-methyl-9-(methylthio)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-4-methoxy- (9CI) (CA INDEX NAME)



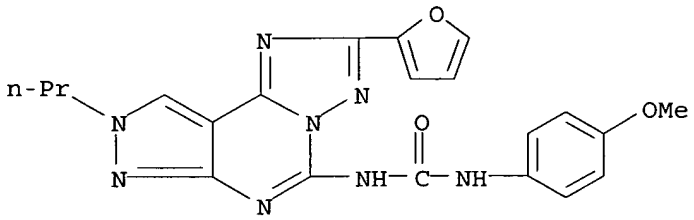
L6 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:867602 CAPLUS
DOCUMENT NUMBER: 140:105664
TITLE: Alteration of A3 adenosine receptors in human neutrophils and low frequency electromagnetic fields
AUTHOR(S): Varani, Katia; Gessi, Stefania; Merighi, Stefania; Iannotta, Valeria; Cattabriga, Elena; Pancaldi, Cecilia; Cadossi, Ruggero; Borea, Pier Andrea
CORPORATE SOURCE: Pharmacology Unit, Department of Clinical and Experimental Medicine, University of Ferrara, Ferrara, 44100, Italy
SOURCE: Biochemical Pharmacology (2003), 66(10), 1897-1906
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study was designed to evaluate the binding and functional characterization of A3 adenosine receptors in human neutrophils exposed to low frequency, low energy, pulsing electromagnetic fields (PEMFs). Great interest has grown concerning the use of PEMF in the clin. practice for

therapeutic purposes strictly correlated with inflammatory conditions. Saturation expts. performed using the high affinity and selective A3 adenosine antagonist 5N-(4-methoxyphenyl-carbamoyl)amino-8-propyl-2-(2-furyl)pyrazolo-[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine ([3H]-MRE 3008F20) revealed a single class of binding sites with similar affinity in control and in PEMF treated human neutrophils (KD = 2.36±0.16 and 2.45±0.15 nM, resp.). PEMFs treatment revealed that the receptor d. was statistically increased (P<0.01) (Bmax = 451±18 and 736±25 fmol mg-1 protein, resp.). Thermodn. data indicated that [3H]-MRE 3008F20 binding in control and in PEMF-treated human neutrophils was entropy and enthalpy driven. Competition of radioligand binding by the high affinity A3 receptor agonists, N6-(3-iodo-benzyl)-2-chloro-adenosine-5'-N-methyluronamide (Cl-IB-MECA) and N6-(3-iodo-benzyl)adenosine-5'-N-methyl-uronamide (IB-MECA), in the absence of PEMFs revealed high and low affinity values similar to those found in the presence of PEMFs. In both exptl. conditions, the addition of GTP 100 μM shifted the competition binding curves of the agonists from a biphasic to a monophasic shape. In functional assays Cl-IB-MECA and IB-MECA were able to inhibit cAMP accumulation and their potencies were statistically increased after exposure to PEMFs. These results indicate in human neutrophils treated with PEMFs the presence of significant alterations in the A3 adenosine receptor d. and functionality.

IT **252979-43-4**, MRE 3008F20
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(alteration of A3 adenosine receptors in human neutrophils and low frequency electromagnetic fields in relation to adenosine A3 receptor antagonist MRE-3008F20 binding in neutrophils was entropy and enthalpy driven)

RN 252979-43-4 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:686358 CAPLUS

DOCUMENT NUMBER: 140:111366

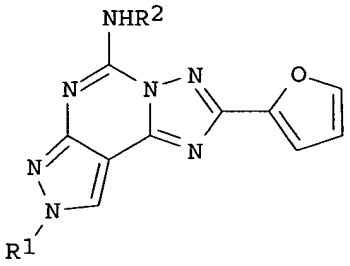
TITLE: New strategies for the synthesis of A3 adenosine receptor antagonists

AUTHOR(S): Baraldi, Pier Giovanni; Bovero, Andrea; Fruttarolo, Francesca; Romagnoli, Romeo; Tabrizi, Mojgan Aghazadeh; Preti, Delia; Varani, Katia; Borea, Pier Andrea; Moorman, Allan R.

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy

SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(19),

4161-4169
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:111366
GI

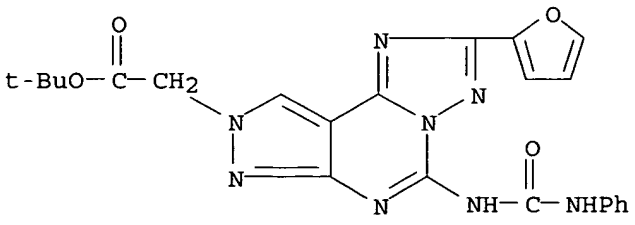


I

AB New A3 adenosine receptor antagonists I [R1 = HO(CH2)2, (EtO)2CHCH2, HO2CCH2, etc.; R2 = H, PhNHCO, 3-ClC6H4NHCO] were synthesized and tested at human adenosine receptor subtypes. An advanced synthetic strategy permitted us to obtain a large amount of the key intermediate I (R1 = R2 = H) that was then submitted to alkylation procedures in order to obtain I [R1 = HO(CH2)2, (EtO)2CHCH2, Me3CO2CCH2, etc.; R2 = H]. The latter were then functionalized into ureas at the 5-position to evaluate their affinity and selectivity vs. hA3 adenosine receptor subtype; in particular, I [R1 = PhCH2O(CH2)2, HO(CH2)2; R2 = PhNHCO] displayed a value of affinity of 4.9 and 1.3 nM, resp. Starting from I (R1 = R2 = H), the synthetic methodologies employed allowed to perform a rapid and a convenient divergent synthesis. This method could be used as a general procedure for the design of novel A3 adenosine receptor antagonists without the difficulty of separating the N8-substituted pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidines from the corresponding N7-isomers.

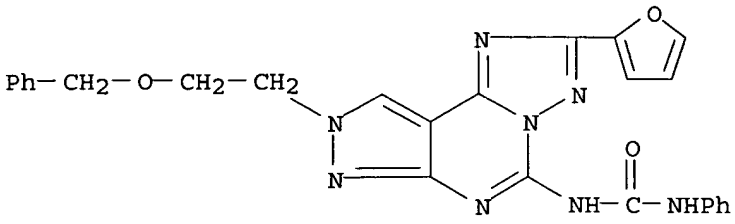
IT **646511-92-4P 646512-01-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino- and ureido-substituted pyrazoltriazolopyrimidines as A3 adenosine receptor antagonists)

RN 646511-92-4 CAPLUS
CN 8H-Pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidine-8-acetic acid, 2-(2-furanyl)-5-[[(phenylamino)carbonyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



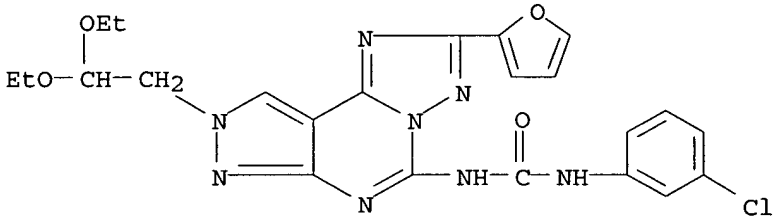
RN 646512-01-8 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-[2-(phenylmethoxy)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)

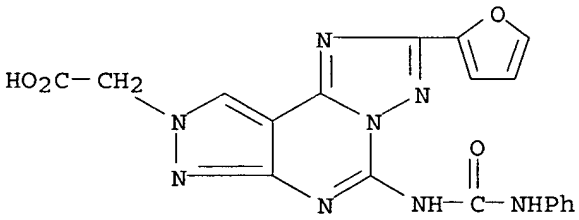


IT **646511-93-5P 646511-94-6P 646512-02-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of amino- and ureido-substituted pyrazoltriazolopyrimidines as A3 adenosine receptor antagonists)

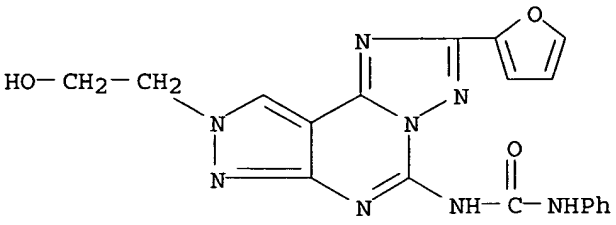
RN 646511-93-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-(2,2-diethoxyethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 646511-94-6 CAPLUS
CN 8H-Pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidine-8-acetic acid, 2-(2-furanyl)-5-[[(phenylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 646512-02-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-hydroxyethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

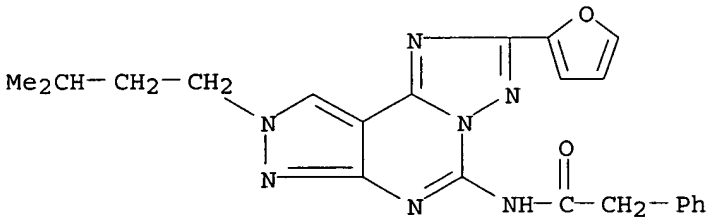
L6 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:679451 CAPLUS
DOCUMENT NUMBER: 139:292225
TITLE: Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine Derivatives as Adenosine Receptor Antagonists. Influence of the N5 Substituent on the Affinity at the Human A3 and A2B Adenosine Receptor Subtypes: A Molecular Modeling Investigation
AUTHOR(S): Pastorin, Giorgia; Da Ros, Tatiana; Spalluto, Giampiero; Deflorian, Francesca; Moro, Stefano; Cacciari, Barbara; Baraldi, Pier Giovanni; Gessi, Stefania; Varani, Katia; Borea, Pier Andrea
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Trieste, Trieste, I-34127, Italy
SOURCE: Journal of Medicinal Chemistry (2003), 46(20), 4287-4296
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:292225

AB A new series of pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines bearing various substituents at both the N5-pyrimidinyl and N8-pyrazolyl positions have been synthesized, and their binding affinities at the four human adenosine receptor subtypes (hA1, hA2A, hA2B, and hA3) have been evaluated. All the described compds. contain arylacetyl moieties at the N5 position and arylalkyl substituents at the N8 position. Surprisingly, all the compds. present their most potent affinities at the hA2B adenosine receptor with a range of selectivities against the other subtypes. When bulky groups are present simultaneously at the N5 and N8 positions [e.e., N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-1-naphthaleneacetamide (I)], the best selectivity for the hA2B receptor was observed (Ki(hA1) = 1100 nM; Ki(hA2A) = 800 nM; Ki(hA2B) = 20 nM; Ki(hA3) = 300 nM, Ki(hA1/A2B) = 55, Ki(hA2A/A2B) = 40, Ki(hA3/hA2B) = 15). To understand the mol. significance of these results, we compared the putative TM (transmembrane) binding motif of I on both hA2B and hA3 receptors. From our docking studies, I fits neatly inside the TM region of the hA2B receptor but not in the corresponding hA3 region, illustrating significant differences between the two subtypes. The study herein presented permits an understanding of why the bioisosteric replacement of an -NH, present in previously reported hA3 receptor antagonists, with a -CH2 group at the N5 position induces such large differences in hA2B/hA3 affinity. In the mol. structure of the hA3 receptor, two residues, Ser243 (TM6) and Ser271 (TM7), create a hydrophilic region, which seems to permit a better accommodation of the phenylurea series into this putative hA3 binding site than the

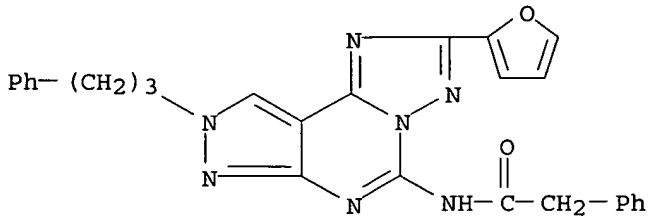
phenylacetyl series.

IT **261629-30-5P**, N-[2-(2-Furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]benzeneacetamide
261629-31-6P, N-[2-(2-Furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]benzeneacetamide
608521-49-9P, N-[2-(2-Furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]benzeneacetamide
608521-50-2P, N-[2-(2-Furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-1-naphthaleneacetamide
608521-51-3P, N-[2-(2-Furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-1-naphthaleneacetamide
608521-52-4P, N-[2-(2-Furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-1-naphthaleneacetamide
608521-53-5P 608521-54-6P 608521-55-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of pyrazolotriazolopyrimidine derivs. as adenosine receptor antagonists; influence of N5 substituent on affinity at human A3 and A2B adenosine receptor subtypes and mol. modeling investigation)

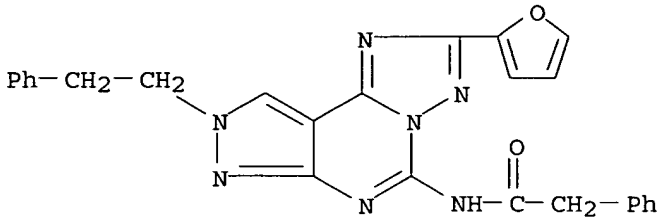
RN 261629-30-5 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



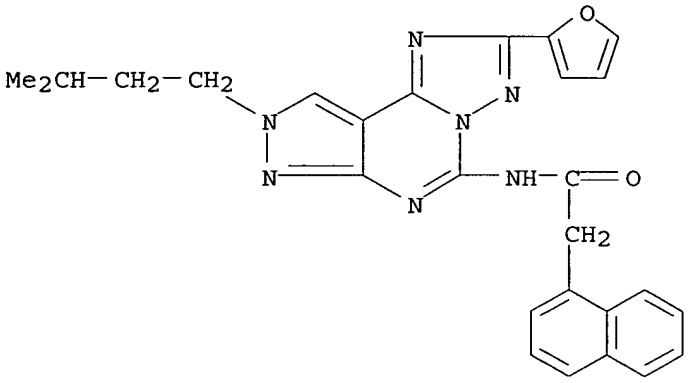
RN 261629-31-6 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



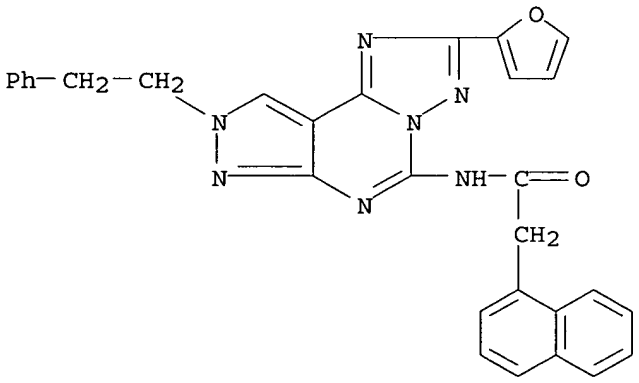
RN 608521-49-9 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



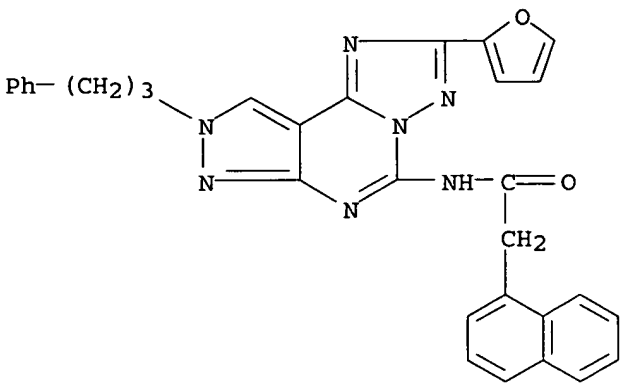
RN 608521-50-2 CAPLUS
CN 1-Naphthaleneacetamide, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



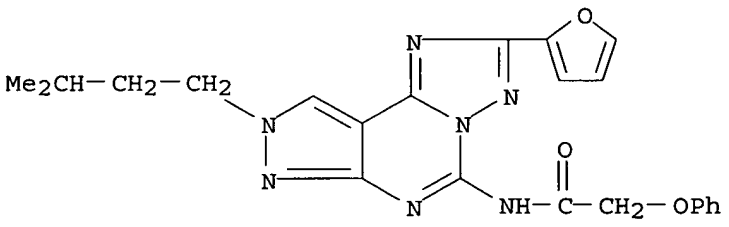
RN 608521-51-3 CAPLUS
CN 1-Naphthaleneacetamide, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



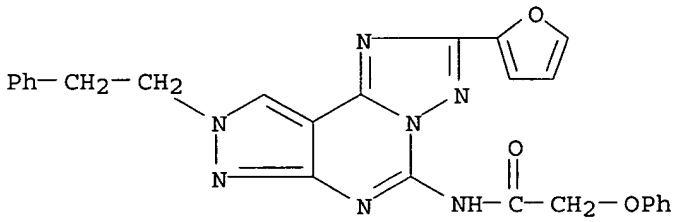
RN 608521-52-4 CAPLUS
CN 1-Naphthaleneacetamide, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



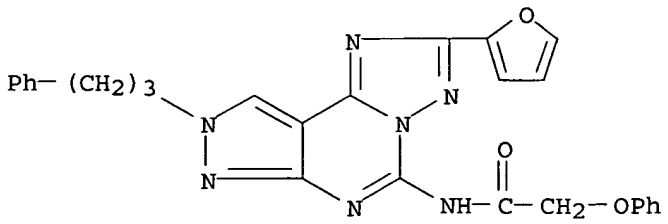
RN 608521-53-5 CAPLUS
CN Acetamide, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-2-phenoxy- (9CI) (CA INDEX NAME)



RN 608521-54-6 CAPLUS
CN Acetamide, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-2-phenoxy- (9CI) (CA INDEX NAME)



RN 608521-55-7 CAPLUS
CN Acetamide, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-2-phenoxy- (9CI) (CA INDEX NAME)



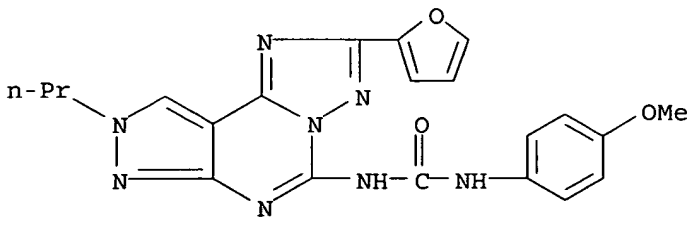
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:669201 CAPLUS
DOCUMENT NUMBER: 140:138838
TITLE: Pyrazolotriazolopyrimidine derivatives sensitize melanoma cells to the chemotherapeutic drugs: taxol and vindesine
AUTHOR(S): Merighi, Stefania; Mirandola, Prisco; Varani, Katia; Gessi, Stefania; Capitani, Silvano; Leung, Edward; Baraldi, Pier Giovanni; Tabrizi, Mojgan Aghazadeh; Borea, Pier Andrea
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Ferrara, 44100, Italy
SOURCE: Biochemical Pharmacology (2003), 66(5), 739-748
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

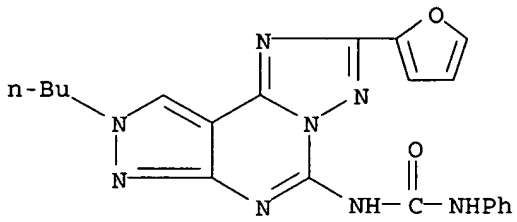
AB In this study, we have evaluated the "in vitro" modulatory activity of a series of pyrazolotriazolopyrimidine derivs. (PTP-d) in sensitizing malignant melanoma cells to the chemotherapeutic drugs: taxol and vindesine. To that end, we have described the impact of chemotherapeutic agents on the cell cycle and on the induction of apoptosis when used alone or in combination with PTP-d. We have demonstrated that four PTP-d reduced chemotherapeutic drugs EC50 doses of the G2/M accumulation with an average of 1.7-fold for taxol and 9.5-fold for vindesine when challenged on A375 human melanoma cell line. This sensitization activity was also confirmed by analyzing the apoptosis degree induced by the chemotherapeutic drugs. Interestingly, PTP-d had no effects on the response to cytotoxic agents by skin-derived human keratinocyte cells, NCTC 2544. Therefore, we have investigated the signaling pathway sustaining the sensitizing effect of PTP-d, providing functional evidence that active compds. are able to inhibit multidrug resistance-associated ATP-binding cassette drug transporter. These results suggested that PTP-d hold great promise for the treatment of multidrug resistance in cancers, leading to potential new therapies for melanoma.

IT **252979-43-4**, MRE 3008F20 **361484-64-2**, MRE 3062F20
396653-58-0, MRE 3046F20 **404011-83-2**, MRE 3042F20
404011-85-4, MRE 3056F20 **638195-75-2**, MRE 3100F20
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrazolotriazolopyrimidine derivs. sensitize melanoma cells to the antitumor drugs, taxol and vindesine)

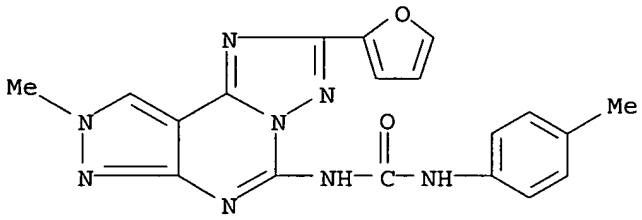
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



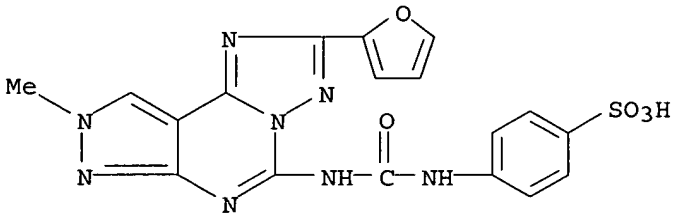
RN 361484-64-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



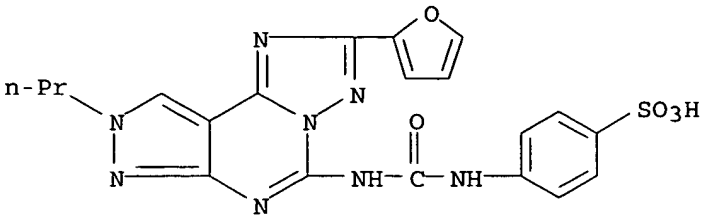
RN 396653-58-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



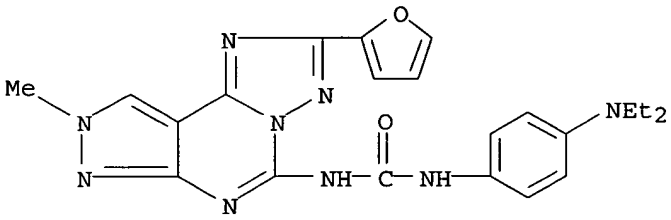
RN 404011-83-2 CAPLUS
CN Benzenesulfonic acid, 4-[[[[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 404011-85-4 CAPLUS
CN Benzenesulfonic acid, 4-[[[[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 638195-75-2 CAPLUS
CN Urea, N-[4-(diethylamino)phenyl]-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:590829 CAPLUS
DOCUMENT NUMBER: 139:133584
TITLE: Preparation of pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidines and analogs as adenosine A3 receptor modulators for therapeutic and diagnostic use
INVENTOR(S): Baraldi, Pier Giovanni; Borea, Pier Andrea
PATENT ASSIGNEE(S): King Pharmaceuticuals Research & Development, Inc., Italy
SOURCE: U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of U.S. 6,407,236.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003144266	A1	20030731	US 2002-134219	20020426
US 6921825	B2	20050726		
US 6448253	B1	20020910	US 1998-154435	19980916
US 6407236	B1	20020618	US 1999-379300	19990823
AU 2002305386	A1	20031111	AU 2002-305386	20020506
CA 2451081	AA	20031120	CA 2002-2451081	20020506
WO 2003095457	A1	20031120	WO 2002-US14191	20020506

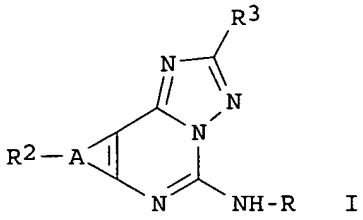
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

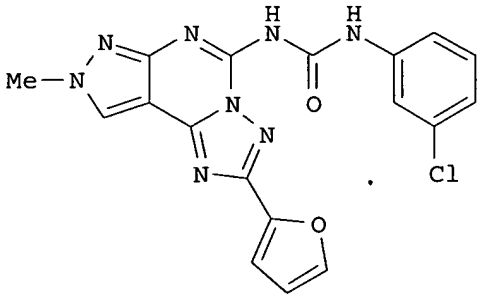
BR 2002010720	A	20040720	BR 2002-10720	20020506
EP 1499614	A1	20050126	EP 2002-734202	20020506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
ZA 200309907	A	20050322	ZA 2003-9907	20020506
JP 2006510574	T2	20060330	JP 2004-503471	20020506
US 2006040959	A1	20060223	US 2005-169311	20050627
PRIORITY APPLN. INFO.:			US 1998-154435	A2 19980916
			US 1999-379300	A2 19990823
			US 2002-134219	A 20020426
			WO 2002-US14191	W 20020506

OTHER SOURCE(S): MARPAT 139:133584

GI



I



II

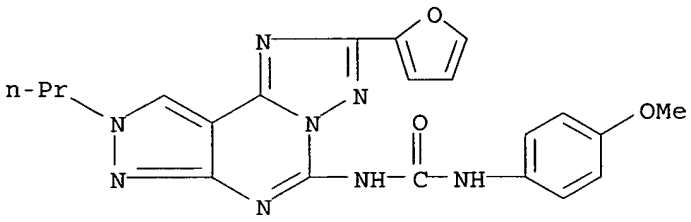
AB Title compds. I [wherein A = imidazole, pyrazole, or triazole; R = CXR1, CXN(R1)2, CXOR1, CXSR1, SOnR1, SOnSR1, or SOnN(R1)2; R1 = H, (hetero)aryl, heterocyclyl, alkanoyl, or (un)substituted alkyl, alkenyl, or alkynyl; or N(R1)2 = azetidinyl or 5-6 membered heterocyclyl; R2 = H or (un)substituted alkyl, alkenyl, aralkyl, or (hetero)aryl; R3 = (un)substituted (benzo)furanyl, (benzo)pyrrolyl, or (benzo)thiophenyl; X = O, S, or NR1; n = 0-2; or pharmaceutically acceptable salts thereof] were prepared as selective A3 adenosine receptor agonists. Thus, 3-amino-1H-pyrazole-4-carbonitrile was methylated, treated with tri-Et orthoformate to give the imidate, and cyclized with 2-furoic acid hydrazide to give 8-methyl-2-(2-furyl)pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine (45%). Amination (53%) and addition of 3-chlorophenyl isocyanate (98%) afforded II, which exhibited binding affinity at the A1, A2, and A3 receptors with Ki values of 5,045 nM, >10,1000 nM, and 0.22 nM, resp. I are useful for the treatment disorders caused by excessive activation of the A3 receptor, such as hypertension, inflammation, mast cell degranulation, cardiac hypoxia, allergic disease, and for protection against cerebral ischemia (no data). In addition, I are useful in diagnostic applications to determine the relative binding of other compds. to the A3 receptor. For instance, the compds. can be labeled, for example with

fluorescent or radiolabels, and the labels used in vivo or in vitro to determine the presence of tumor cells which possess a high concentration of adenosine
A3 receptors.

IT **261629-32-7**, Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-, labeled with tritium
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A3 receptor agonist; preparation of pyrazolotriazolopyrimidine and analogs as adenosine A3 receptor agonists for therapeutic and diagnostic use)

RN 261629-32-7 CAPLUS

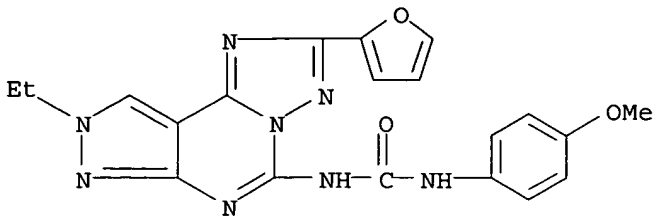
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-, labeled with tritium (9CI) (CA INDEX NAME)



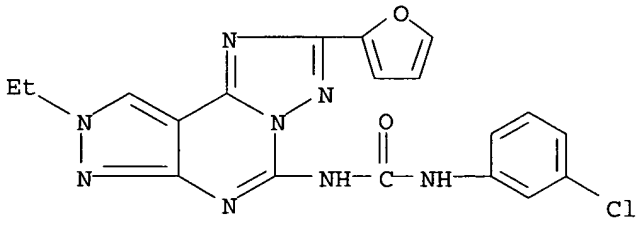
IT **252979-41-2P**, Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
252979-42-3P, Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
252979-43-4P, Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
252979-44-5P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
252979-45-6P, Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
252979-46-7P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
252979-47-8P, Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
252979-48-9P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
261629-22-5P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
261629-23-6P, Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
261629-24-7P, Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-chlorophenyl)-
261629-25-8P, Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
261629-26-9P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
261629-27-0P, Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
261629-28-1P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
261629-29-2P, Urea, N-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-

261629-30-5P, Benzeneacetamide, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
261629-31-6P, Benzeneacetamide, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(A3 receptor agonist; preparation of pyrazolotriazolopyrimidine and analogs as adenosine A3 receptor agonists for therapeutic and diagnostic use)

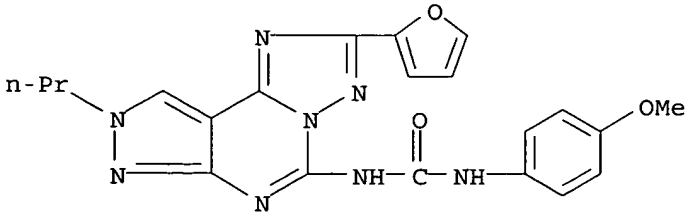
RN 252979-41-2 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



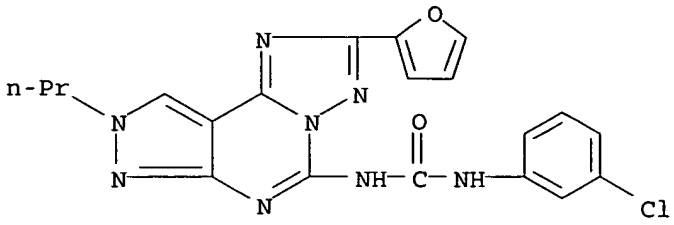
RN 252979-42-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



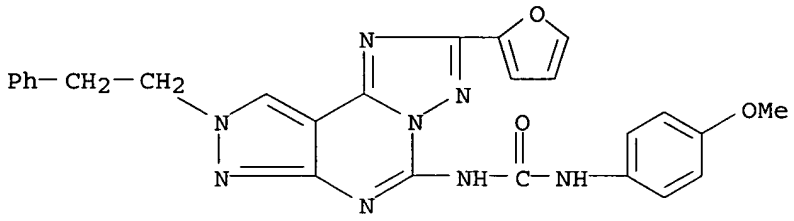
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



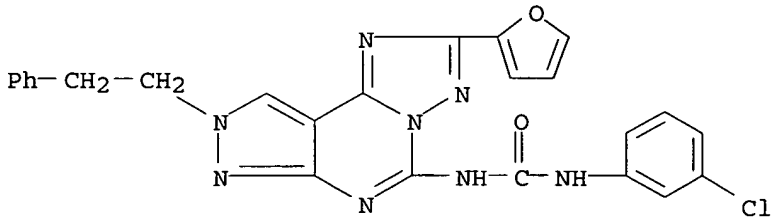
RN 252979-44-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



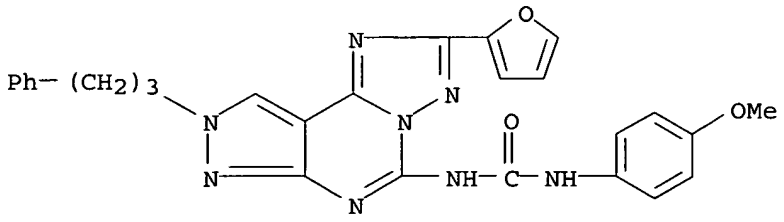
RN 252979-45-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 252979-46-7 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

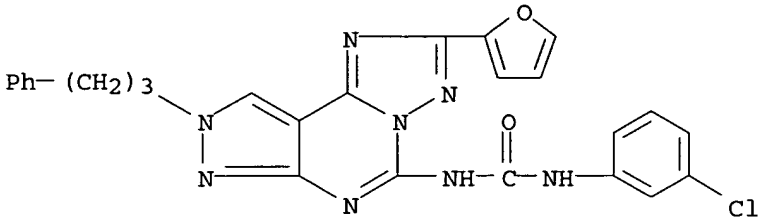


RN 252979-47-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

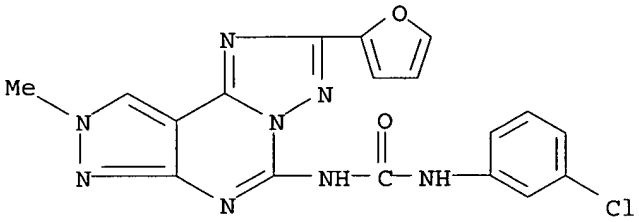


RN 252979-48-9 CAPLUS

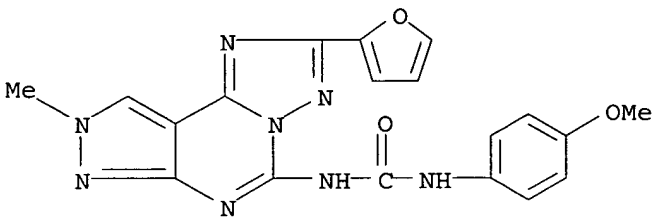
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



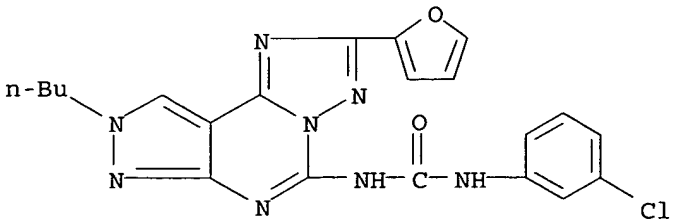
RN 261629-22-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



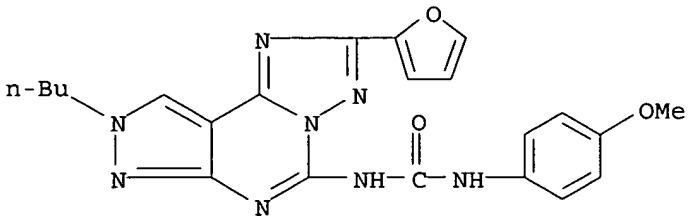
RN 261629-23-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



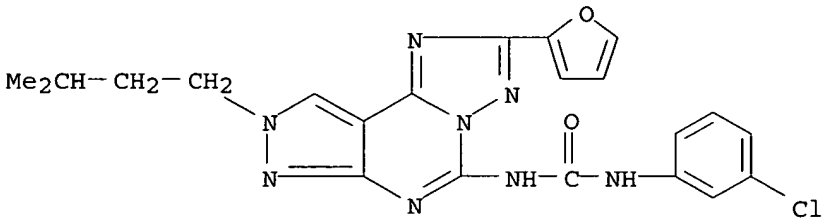
RN 261629-24-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



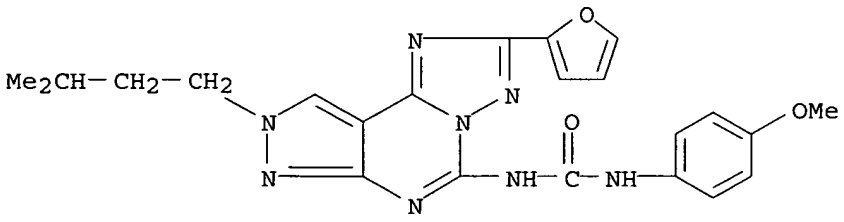
RN 261629-25-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



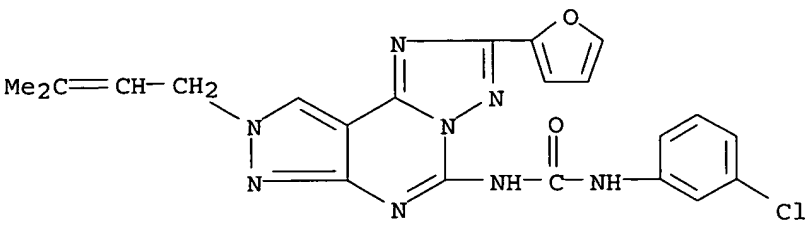
RN 261629-26-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



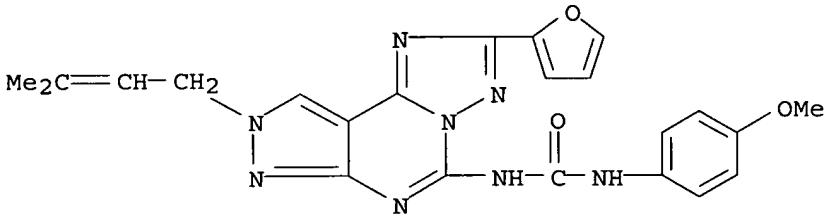
RN 261629-27-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



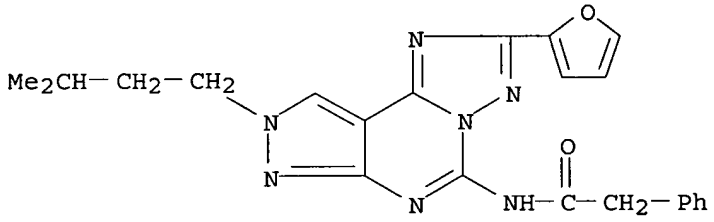
RN 261629-28-1 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



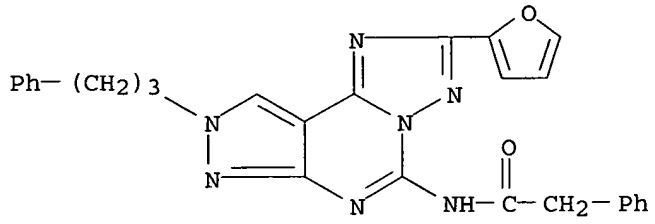
RN 261629-29-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 261629-30-5 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



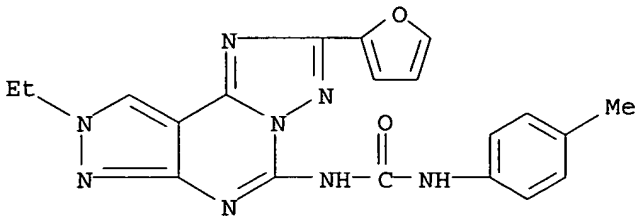
RN 261629-31-6 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



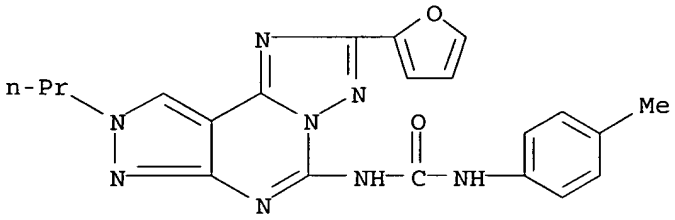
IT **404011-49-0P 404011-60-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of pyrazolotriazolopyrimidine and analogs as adenosine A3 receptor agonists for therapeutic and diagnostic use)

RN 404011-49-0 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



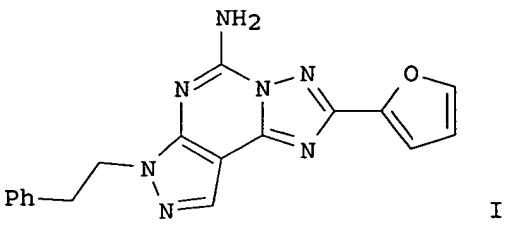
RN 404011-60-5 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:151162 CAPLUS
DOCUMENT NUMBER: 138:321211
TITLE: Design, Synthesis, and Biological Evaluation of C9- and C2-Substituted Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines as New A2A and A3 Adenosine Receptor Antagonists
AUTHOR(S): Baraldi, Pier Giovanni; Fruttarolo, Francesca; Tabrizi, Mojgan Aghazadeh; Preti, Delia; Romagnoli, Romeo; El-Kashef, Hussein; Moorman, Allan; Varani, Katia; Gessi, Stefania; Merighi, Stefania; Borea, Pier Andrea
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche and Dipartimento di Medicina Clinica e Sperimentale-Sezione di Farmacologia, Universita di Ferrara, Ferrara, 44100, Italy
SOURCE: Journal of Medicinal Chemistry (2003), 46(7), 1229-1241
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:321211

GI



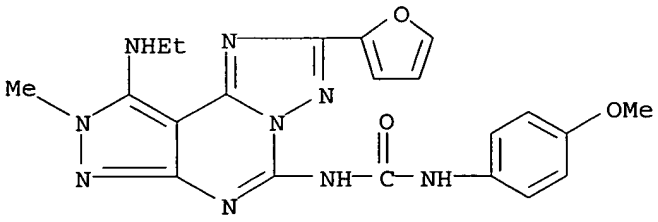
I

AB Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines such as I are prepared as selective adenosine A2a and A3 receptor antagonists. Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines substituted at the 9-position retain receptor affinity but lose selectivity for the adenosine A2a and A3 receptors over other adenosine receptors. Replacement of the furan moiety present in the pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine with a Ph or a substituted aromatic ring abolishes affinity at all the adenosine receptor subtypes, demonstrating that the furanyl ring is a necessary structural element to guarantee interaction with the adenosine receptor surface; replacement of the furan ring with an ortho-ethoxy-substituted aromatic ring did not enhance affinity. Introduction of a N-methylpiperazinomethyl or morpholinomethyl function at the 5' position of the furanyl ring of I or introduction of a methylsulfanyl moiety at the 9-position of pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines yields inhibitors with improved water solubilities but reduced affinities for adenosine A2a and A3 receptors.

IT **512846-16-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and structure-activity relationships of pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines as potential selective adenosine A2a and A3 receptor antagonists)

RN 512846-16-1 CAPLUS

CN Urea, N-[9-(ethylamino)-2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

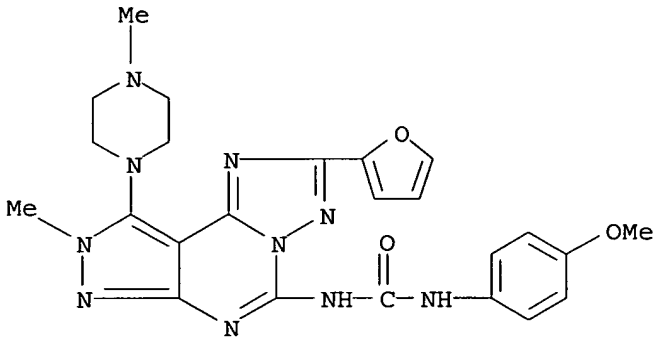


IT **512846-18-3P 512846-20-7P 512846-22-9P**
512846-24-1P 512846-26-3P 512846-28-5P
512846-38-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity relationships of pyrazolo[4,3-e]-1,2,4-

triazolo[1,5-c]pyrimidines as potential selective adenosine A2a and A3 receptor antagonists)

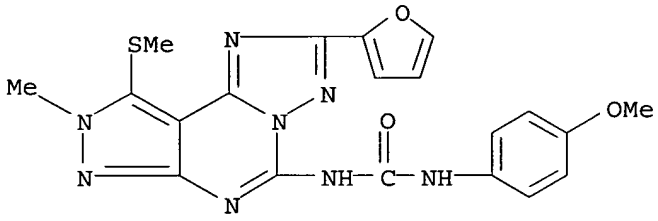
RN 512846-18-3 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-methyl-9-(4-methyl-1-piperazinyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



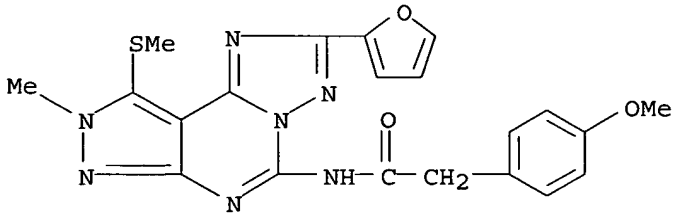
RN 512846-20-7 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-methyl-9-(methylthio)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



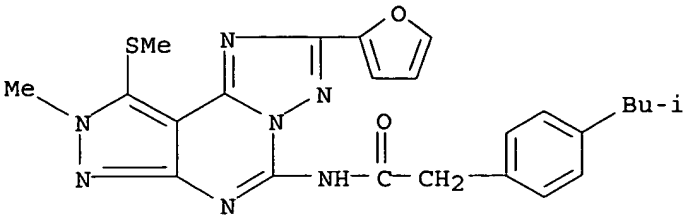
RN 512846-22-9 CAPLUS

CN Benzeneacetamide, N-[2-(2-furanyl)-8-methyl-9-(methylthio)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-4-methoxy- (9CI) (CA INDEX NAME)

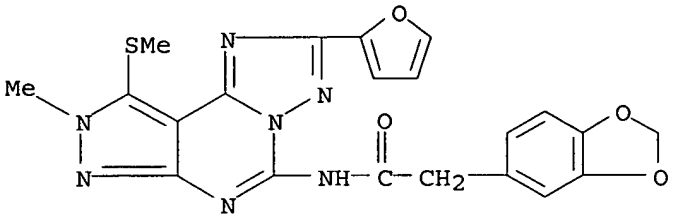


RN 512846-24-1 CAPLUS

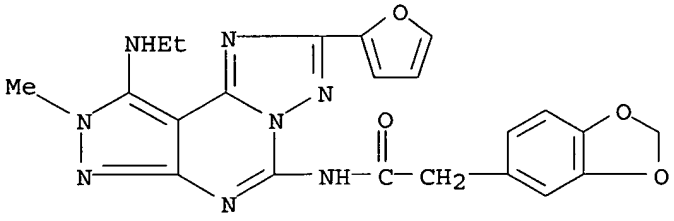
CN Benzeneacetamide, N-[2-(2-furanyl)-8-methyl-9-(methylthio)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



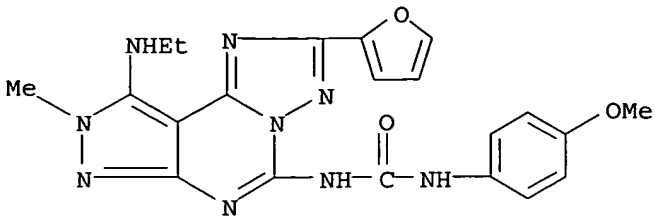
RN 512846-26-3 CAPLUS
CN 1,3-Benzodioxole-5-acetamide, N-[2-(2-furanyl)-8-methyl-9-(methylthio)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 512846-28-5 CAPLUS
CN 1,3-Benzodioxole-5-acetamide, N-[9-(ethylamino)-2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



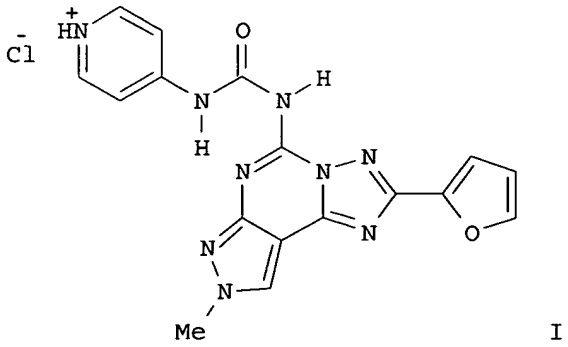
RN 512846-38-7 CAPLUS
CN Urea, N-[9-(ethylamino)-2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:532124 CAPLUS
DOCUMENT NUMBER: 137:232616
TITLE: Synthesis, Biological Properties, and Molecular Modeling Investigation of the First Potent, Selective, and Water-Soluble Human A3 Adenosine Receptor Antagonist
AUTHOR(S): Maconi, Anna; Pastorin, Giorgia; Da Ros, Tatiana; Spalluto, Giampiero; Gao, Zhan-guo; Jacobson, Kenneth A.; Baraldi, Pier Giovanni; Cacciari, Barbara; Varani, Katia; Moro, Stefano; Borea, Pier Andrea
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Trieste, Trieste, I-34127, Italy
SOURCE: Journal of Medicinal Chemistry (2002), 45(17), 3579-3582
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:232616
GI



I

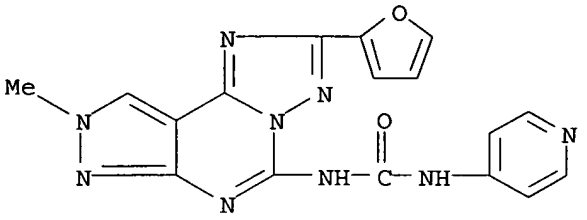
AB A new, highly potent, selective, and water-soluble antagonist of the hA3 adenosine receptor was synthesized and tested in binding and functional assays. Pyridyl substituted pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine hydrochloride I displayed high water solubility (15 mM) and the

highest affinity (Ki = 0.01 nM) and selectivity for the hA3 vs. A1, A2A, and A2B receptors (>10000-fold) ever reported. A Schild anal. of the antagonism by I of agonist-induced inhibition of cAMP production in CHO cells expressing the hA3 receptor indicated a KB value of 0.20 nM.

IT **458556-53-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and mol. modeling study of pyridyl-substituted pyrazolotriazolopyrimidine as selective, water-soluble human A3 adenosine receptor antagonist)

RN 458556-53-1 CAPLUS

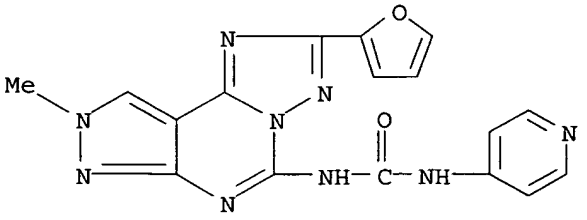
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-4-pyridinyl- (9CI) (CA INDEX NAME)



IT **458556-54-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and mol. modeling study of pyridyl-substituted pyrazolotriazolopyrimidine as selective, water-soluble human A3 adenosine receptor antagonist)

RN 458556-54-2 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-4-pyridinyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:461311 CAPLUS
DOCUMENT NUMBER: 137:33313
TITLE: Preparation of pyrazolo[4,3-e]1,2,4-triazolo[1,5-

c]pyrimidines and analogs as adenosine A3 receptor modulators for therapeutic and diagnostic use

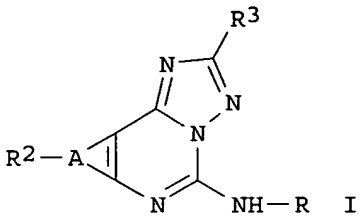
INVENTOR(S): Baraldi, Pier Giovanni; Borea, Pier Andrea
PATENT ASSIGNEE(S): Medco Research, Inc., USA
SOURCE: U.S., 30 pp., Cont.-in-part of U.S. Ser. No. 154,435.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6407236	B1	20020618	US 1999-379300	19990823
US 6448253	B1	20020910	US 1998-154435	19980916
CA 2332007	AA	20000323	CA 1999-2332007	19990915
WO 2000015231	A1	20000323	WO 1999-US21103	19990915
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9962482	A1	20000403	AU 1999-62482	19990915
AU 749211	B2	20020620		
GB 2353527	A1	20010228	GB 2000-27879	19990915
GB 2353527	B2	20040225		
BR 9913766	A	20010605	BR 1999-13766	19990915
TR 200003461	T2	20010621	TR 2000-200003461	19990915
DE 19983530	T	20011108	DE 1999-19983530	19990915
CH 692132	A	20020228	CH 1999-1201	19990915
JP 2002524519	T2	20020806	JP 2000-569815	19990915
NZ 509149	A	20030829	NZ 1999-509149	19990915
ES 2204262	A1	20040416	ES 2001-50007	19990915
ES 2204262	B1	20050301		
SE 2000003984	A	20001222	SE 2000-3984	20001101
SE 522578	C2	20040217		
NO 2000005508	A	20010315	NO 2000-5508	20001101
NO 318078	B1	20050131		
LU 90687	A1	20001219	LU 2000-90687	20001206
ZA 2001001626	A	20011213	ZA 2001-1626	20010227
HK 1035671	A1	20050218	HK 2001-106364	20010907
US 2003144266	A1	20030731	US 2002-134219	20020426
US 6921825	B2	20050726		
US 2006040959	A1	20060223	US 2005-169311	20050627

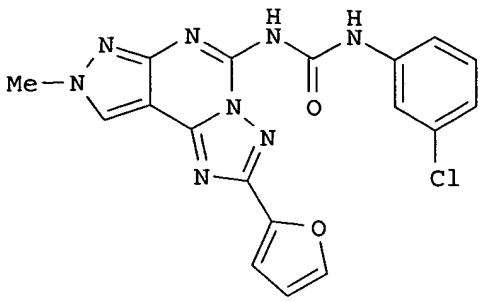
PRIORITY APPLN. INFO.:

US 1998-154435	A2	19980916
US 1999-379300	A	19990823
WO 1999-US21103	W	19990915
US 2002-134219	A3	20020426

OTHER SOURCE(S): MARPAT 137:33313
GI



I



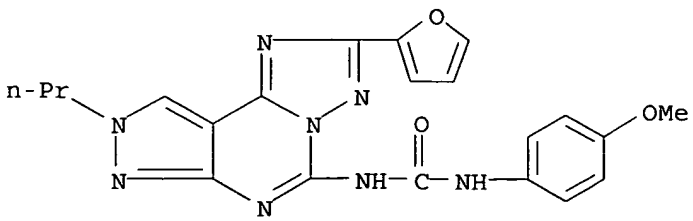
II

AB Title compds. I [wherein A = imidazole, pyrazole, or triazole; R = CXR1, CXN(R1)2, CXOR1, CXSR1, SOnR1, SOnSR1, or SOnN(R1)2; R1 = H, (hetero)aryl, heterocyclyl, alkanoyl, or (un)substituted alkyl, alkenyl, or alkynyl; or N(R1)2 = azetidinyl or 5-6 membered heterocyclyl; R2 = H or (un)substituted alkyl, alkenyl, aralkyl, or (hetero)aryl; R3 = (un)substituted (benzo)furanyl, (benzo)pyrrolyl, or (benzo)thiophenyl; X = O, S, or NR1; n = 0-2; or pharmaceutically acceptable salts thereof] were prepared as selective A3 adenosine receptor agonists. Thus, 3-amino-1H-pyrazole-4-carbonitrile was methylated, treated with tri-Et orthoformate to give the imidate, and cyclized with 2-furoic acid hydrazide to give 8-methyl-2-(2-furyl)pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine (45%). Amination (53%) and addition of 3-chlorophenyl isocyanate (98%) afforded II, which exhibited binding affinity at the A1, A2, and A3 receptors with Ki values of 5,045 nM, >10,1000 nM, and 0.22 nM, resp. I are useful for the treatment disorders caused by excessive activation of the A3 receptor, such as hypertension, inflammation, mast cell degranulation, cardiac hypoxia, allergic disease, and for protection against cerebral ischemia (no data). In addition, I are useful in diagnostic applications to determine the relative binding of other compds. to the A3 receptor. For instance, the compds. can be labeled, for example with fluorescent or radiolabels, and the labels used in vivo or in vitro to determine the presence of tumor cells which possess a high concentration of adenosine
A3 receptors.

IT **261629-32-7**, Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-, labeled with tritium
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A3 receptor agonist; preparation of pyrazolotriazolopyrimidine and analogs as adenosine A3 receptor agonists for therapeutic and diagnostic use)

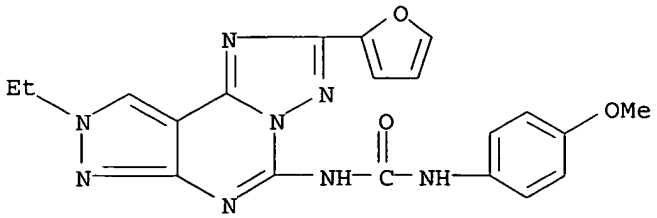
RN 261629-32-7 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-, labeled with tritium (9CI) (CA INDEX NAME)

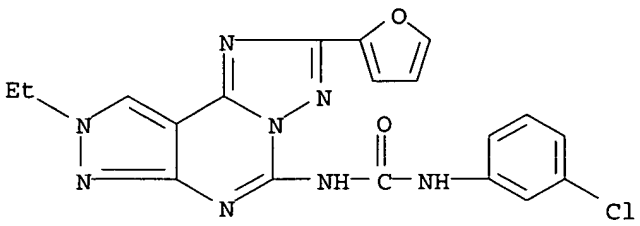


IT **252979-41-2P**, Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
252979-42-3P, Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
252979-43-4P, Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
252979-44-5P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
252979-45-6P, Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
252979-46-7P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
252979-47-8P, Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
252979-48-9P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
261629-22-5P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
261629-23-6P, Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
261629-24-7P, Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-chlorophenyl)-
261629-25-8P, Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
261629-26-9P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
261629-27-0P, Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
261629-28-1P, Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
261629-29-2P, Urea, N-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-
261629-30-5P, Benzeneacetamide, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
261629-31-6P, Benzeneacetamide, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(A3 receptor agonist; preparation of pyrazolotriazolopyrimidine and analogs as adenosine A3 receptor agonists for therapeutic and diagnostic use)

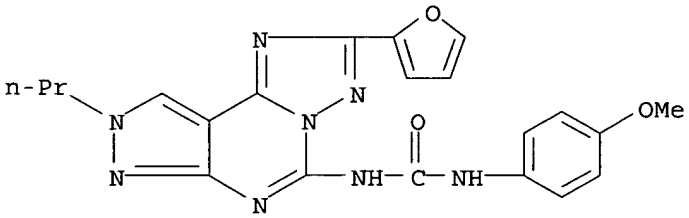
RN 252979-41-2 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



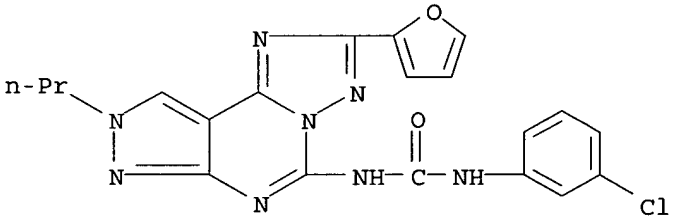
RN 252979-42-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



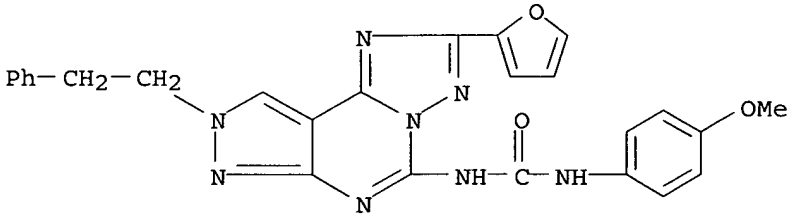
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 252979-44-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

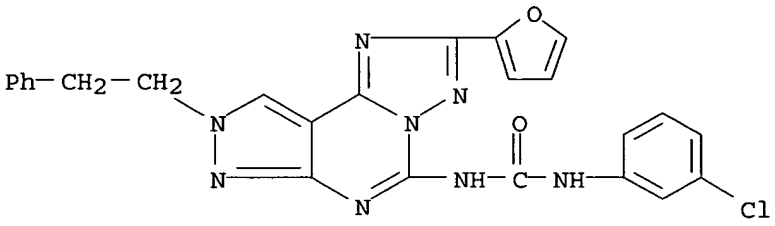


RN 252979-45-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

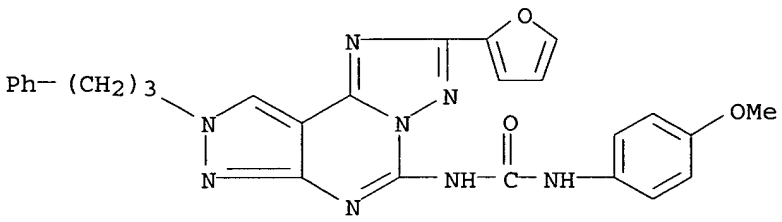


RN 252979-46-7 CAPLUS

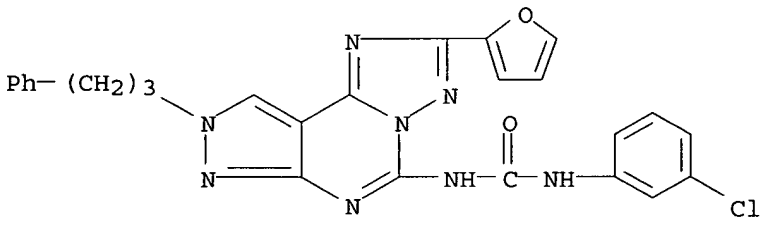
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



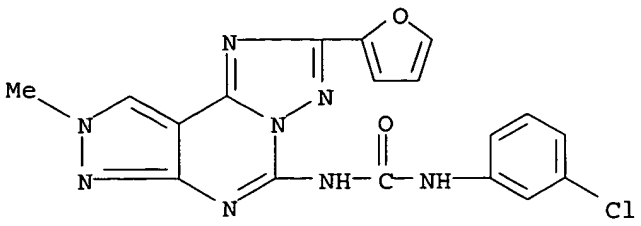
RN 252979-47-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



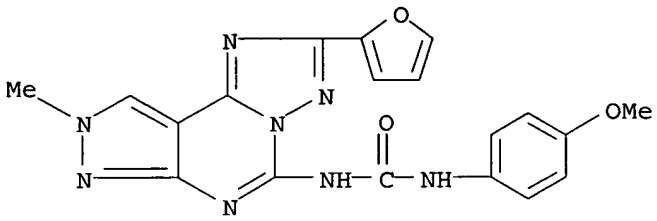
RN 252979-48-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



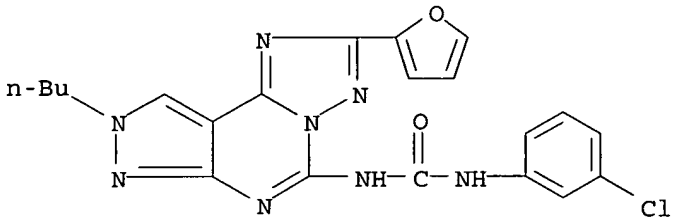
RN 261629-22-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



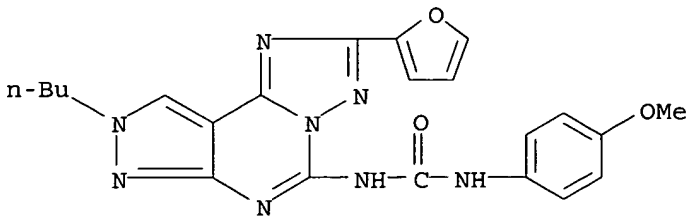
RN 261629-23-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



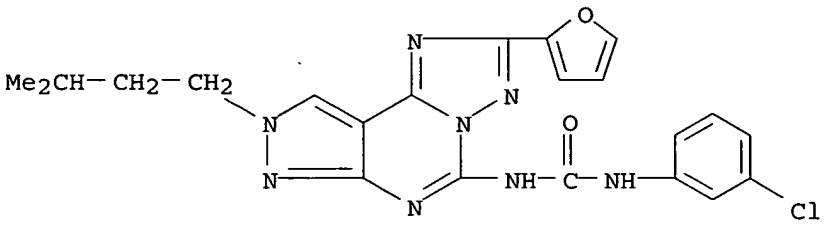
RN 261629-24-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



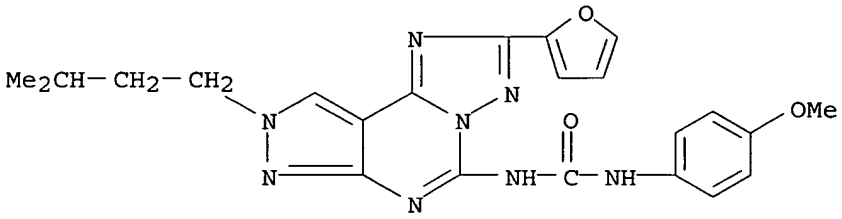
RN 261629-25-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



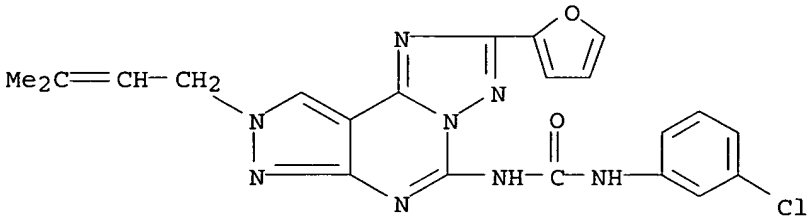
RN 261629-26-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



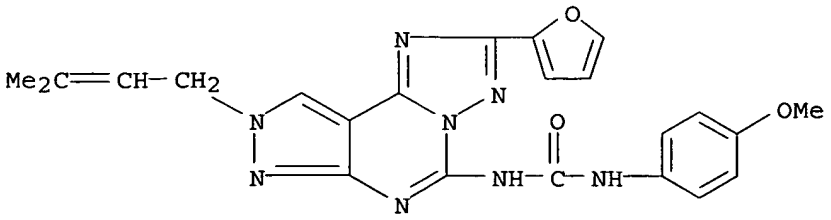
RN 261629-27-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



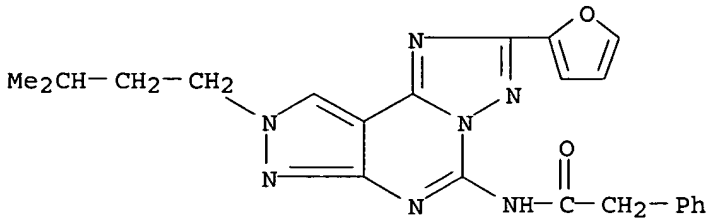
RN 261629-28-1 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



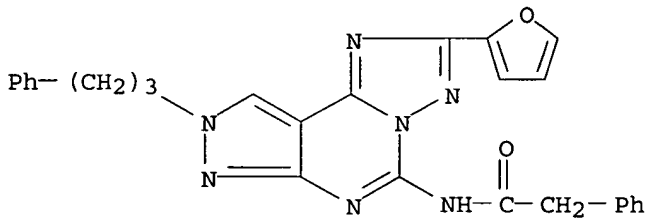
RN 261629-29-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 261629-30-5 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 261629-31-6 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

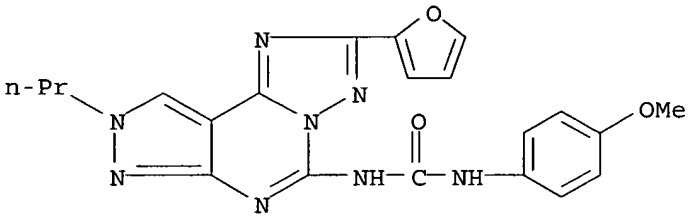
L6 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:119023 CAPLUS
DOCUMENT NUMBER: 136:380449
TITLE: Binding thermodynamics at the human A3 adenosine receptor
AUTHOR(S): Merighi, Stefania; Varani, Katia; Gessi, Stefania; Klotz, Karl-Norbert; Leung, Edward; Baraldi, Pier Giovanni; Borea, Pier Andrea
CORPORATE SOURCE: Pharmacology Unit, Department of Clinical and Experimental Medicine, Centro Nazionale di Eccellenza per lo Sviluppo di Metodologie Innovative per lo Studio ed il Trattamento delle Patologie Infiammatorie, University of Ferrara, Ferrara, 44100, Italy
SOURCE: Biochemical Pharmacology (2002), 63(2), 157-161
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The thermodn. parameters ΔG°, ΔH° and ΔS° of the binding equilibrium of six adenosine receptor agonists and five antagonists at adenosine A3 receptors were determined by means of affinity measurements at six different temps. (4, 10, 15, 20, 25 and 30°) and van't Hoff plots were constructed. Affinity consts. were measured on Chinese hamster ovary (CHO) cells transfected with the human A3 receptors by inhibition assays of the binding of the selective A3

antagonist [3H]MRE 3008F20. The van't Hoff plots were linear for agonists and antagonists in the temperature range 4-30°. Their thermodn. parameters fall in the ranges 21≤ΔH°≤67 kJ mol-1 and 208≤ΔS°≤410 J (K mol)-1 for agonists and -52≤ΔH°≤-9 kJ mol-1 and 16≤ΔS°≤81 J (K/mol)-1 for antagonists, showing that agonist binding is always totally entropy-driven while antagonist binding is enthalpy- and entropy-driven. The results are discussed with the aim of obtaining new details on the nature of the forces driving the A3 binding at a mol. level.

IT **252979-43-4**, MRE 3008F20
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(binding thermodn. at the human A3 adenosine receptor)

RN 252979-43-4 CAPLUS

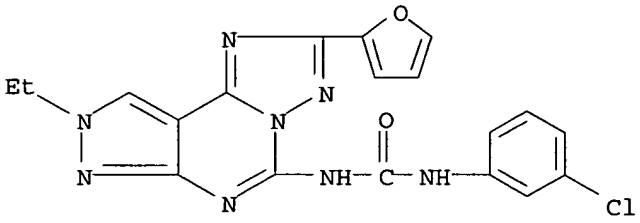
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



IT **252979-42-3**, MRE 3020F20 **252979-45-6**, MRE 3005F20
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(binding thermodn. at the human A3 adenosine receptor)

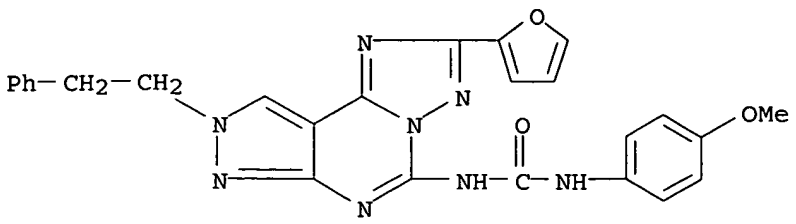
RN 252979-42-3 CAPLUS

CN Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 252979-45-6 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

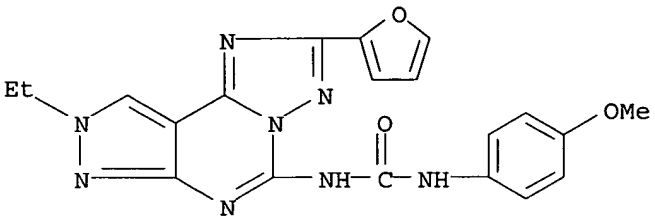
L6 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:27221 CAPLUS
DOCUMENT NUMBER: 136:241075
TITLE: Synthesis, Biological Activity, and Molecular Modeling Investigation of New Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine Derivatives as Human A3 Adenosine Receptor Antagonists
AUTHOR(S): Baraldi, Pier Giovanni; Cacciari, Barbara; Moro, Stefano; Spalluto, Giampiero; Pastorin, Giorgia; Da Ros, Tatiana; Klotz, Karl-Norbert; Varani, Katia; Gessi, Stefania; Borea, Pier Andrea
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche and Dipartimento di Medicina Clinica e Sperimentale-Sezione di Farmacologia, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Journal of Medicinal Chemistry (2002), 45(4), 770-780
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:241075

AB A new series of pyrazolotriazolopyrimidines bearing different substitutions on the phenylcarbamoyl moieties at the N5 position, being highly potent and selective human A3 adenosine receptor antagonists, is described. The compds. represent an extension and an improvement of our previous work on this class of compds. (J. Med. Chemical 1999, 42, 4473-4478; J. Med. Chemical 2000, 43, 4768-4780). All the synthesized compds. showed A3 adenosine receptor affinity in the subnanomolar range and high levels of selectivity in radioligand binding assays at the human A1, A2A, A2B, and A3 adenosine receptors. In particular, the effect of the substitution and its position on the Ph ring have been studied. From binding data, it is evident that the unsubstituted derivs. on the Ph ring (e.g., compound 59, hA3 = 0.16 nM, hA1/hA3 = 3713, hA2A/hA3 = 2381, hA2B/hA3 = 1388) showed the best profile in terms of affinity and selectivity at the human A3 adenosine receptors. The introduction of a sulfonic acid moiety at the para position on the Ph ring was attempted in order to design water soluble derivs. However, this substitution led to a dramatic decrease of affinity at all four adenosine receptor subtypes. A computer-generated model of the human A3 receptor was built and analyzed to better interpret these results, demonstrating that steric control, in particular at the para position on the Ph ring, plays a fundamental role in the receptor interaction. Some of the synthesized compds. proved to be full antagonists in a specific functional model, where the inhibition of cAMP-generation by IB-MECA was measured in membranes of CHO cells stably transfected with the human A3 receptor with IC50 values in the nanomolar range, with a statistically significative linear relationship with the

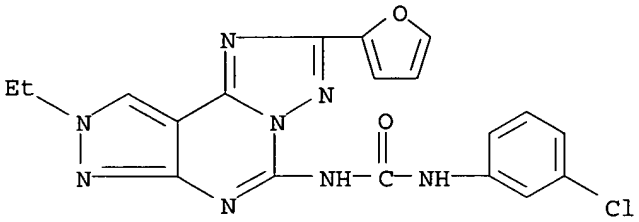
binding data.

IT **252979-41-2 252979-42-3 252979-43-4**
252979-44-5 261629-22-5 261629-23-6
261629-24-7 261629-25-8
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(synthesis, biol. activity, and mol. modeling investigation of new pyrazolotriazolopyrimidine derivs. as human A3 adenosine receptor antagonists)

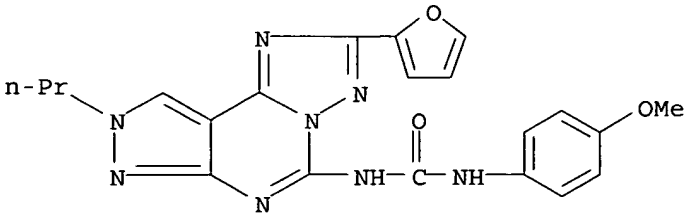
RN 252979-41-2 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



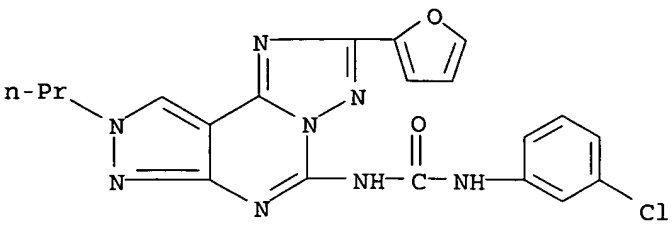
RN 252979-42-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



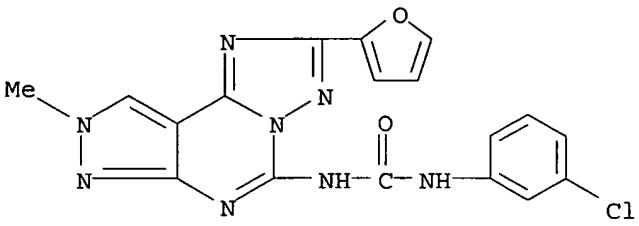
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



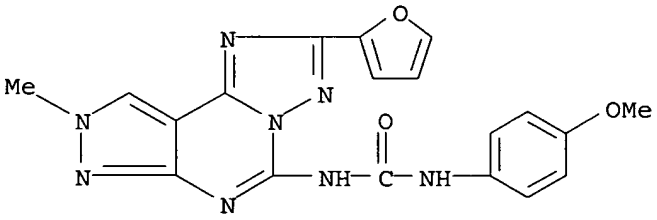
RN 252979-44-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



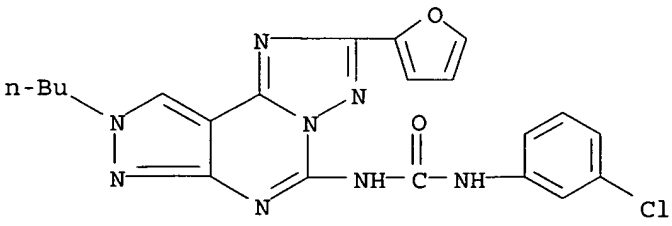
RN 261629-22-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



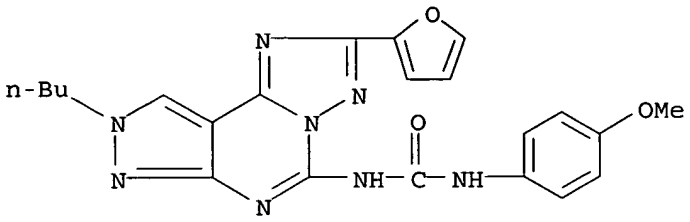
RN 261629-23-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 261629-24-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-chlorophenyl)- (9CI) (CA INDEX NAME)

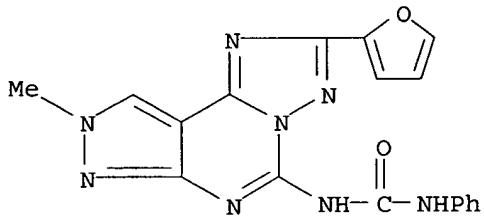


RN 261629-25-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

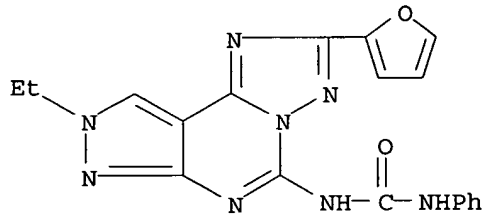


IT **361484-61-9P 361484-62-0P 361484-63-1P**
361484-64-2P
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, biol. activity, and mol. modeling investigation of new pyrazolotriazolopyrimidine derivs. as human A3 adenosine receptor antagonists)

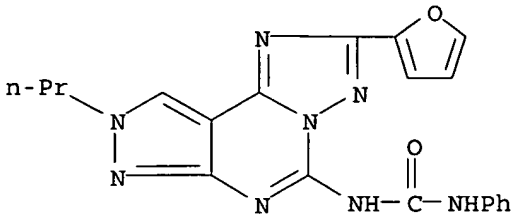
RN 361484-61-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



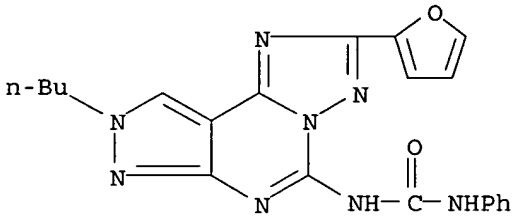
RN 361484-62-0 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



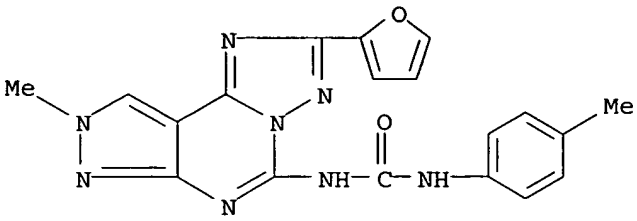
RN 361484-63-1 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



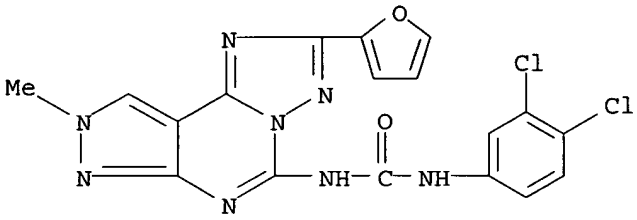
RN 361484-64-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



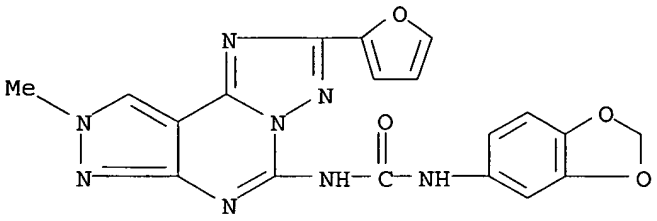
IT **396653-58-0P 404011-36-5P 404011-37-6P**
404011-38-7P 404011-39-8P 404011-40-1P
404011-41-2P 404011-42-3P 404011-43-4P
404011-44-5P 404011-45-6P 404011-46-7P
404011-47-8P 404011-48-9P 404011-49-0P
404011-50-3P 404011-51-4P 404011-52-5P
404011-53-6P 404011-54-7P 404011-55-8P
404011-56-9P 404011-57-0P 404011-58-1P
404011-59-2P 404011-60-5P 404011-61-6P
404011-62-7P 404011-63-8P 404011-64-9P
404011-65-0P 404011-66-1P 404011-67-2P
404011-68-3P 404011-69-4P 404011-70-7P
404011-71-8P 404011-72-9P 404011-73-0P
404011-74-1P 404011-75-2P 404011-76-3P
404011-77-4P 404011-78-5P 404011-79-6P
404011-80-9P 404011-81-0P 404011-82-1P
404011-83-2P 404011-84-3P 404011-85-4P
404011-86-5P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, biol. activity, and mol. modeling investigation of new pyrazolotriazolopyrimidine derivs. as human A3 adenosine receptor antagonists)
RN 396653-58-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



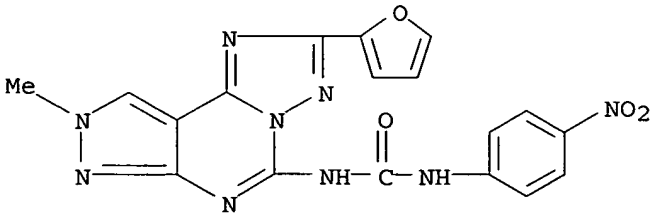
RN 404011-36-5 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



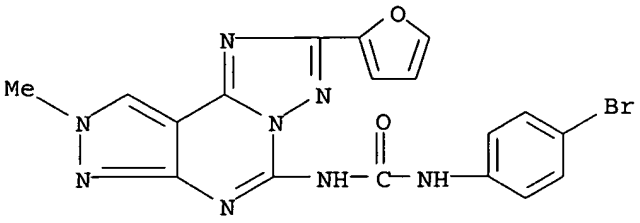
RN 404011-37-6 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



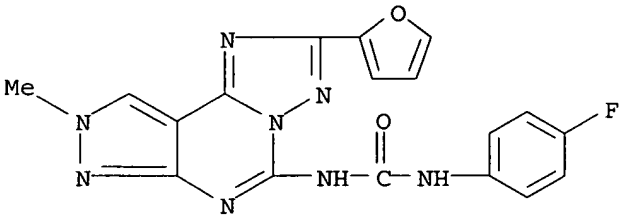
RN 404011-38-7 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



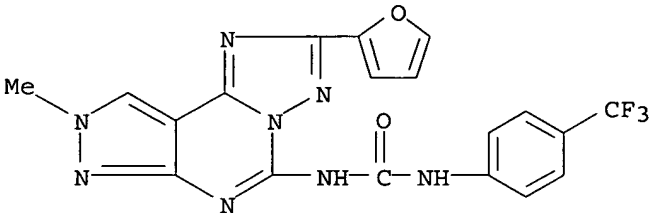
RN 404011-39-8 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



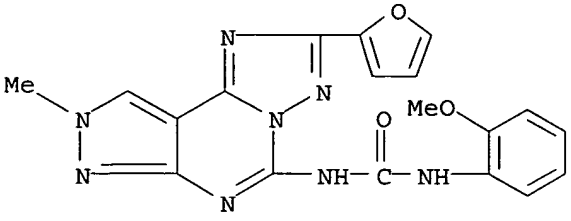
RN 404011-40-1 CAPLUS
CN Urea, N-(4-fluorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



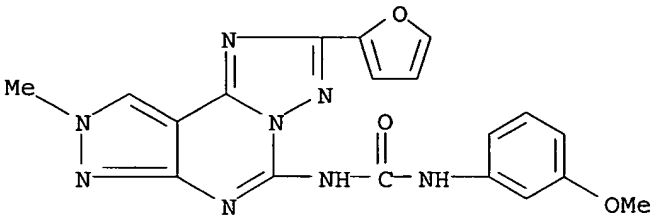
RN 404011-41-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



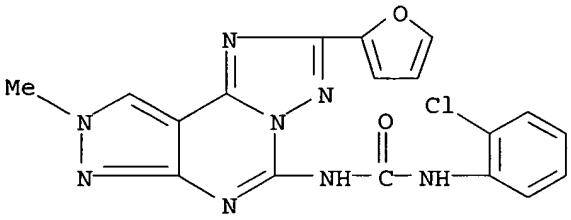
RN 404011-42-3 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



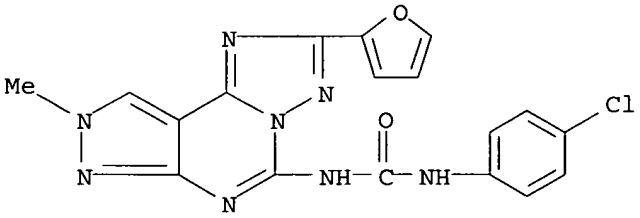
RN 404011-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



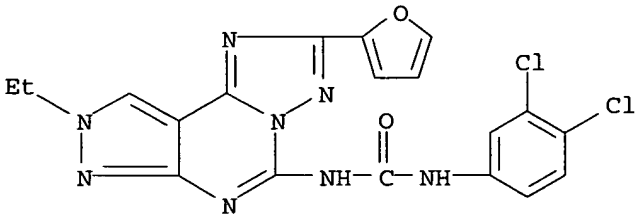
RN 404011-44-5 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 404011-45-6 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

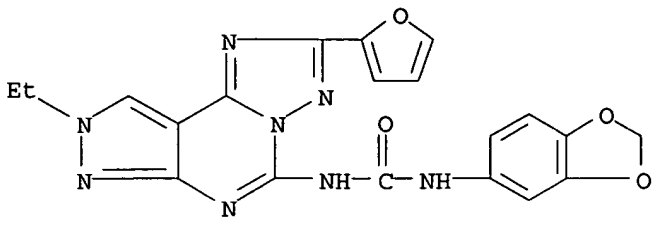


RN 404011-46-7 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

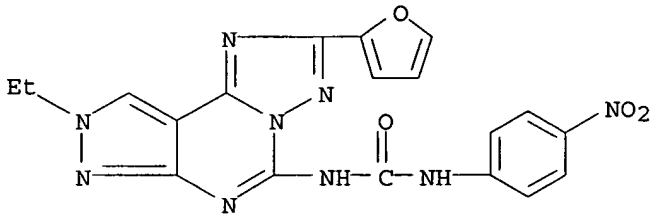


RN 404011-47-8 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-

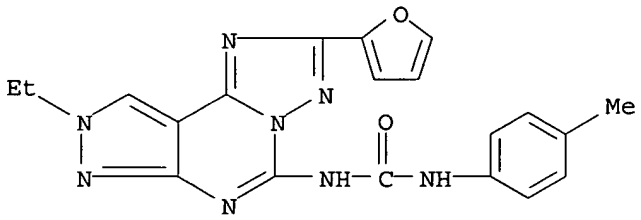
e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



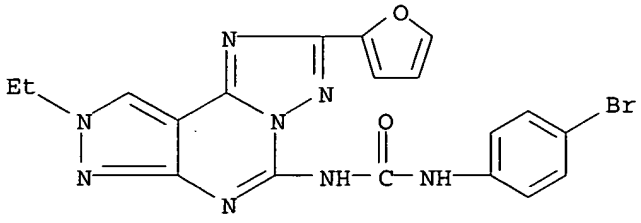
RN 404011-48-9 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



RN 404011-49-0 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)

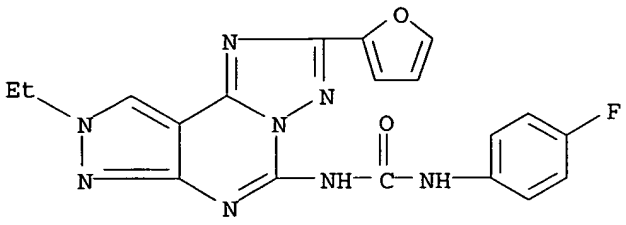


RN 404011-50-3 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

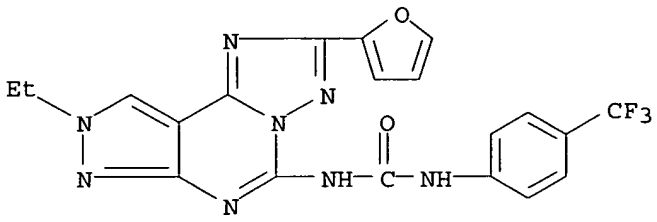


RN 404011-51-4 CAPLUS

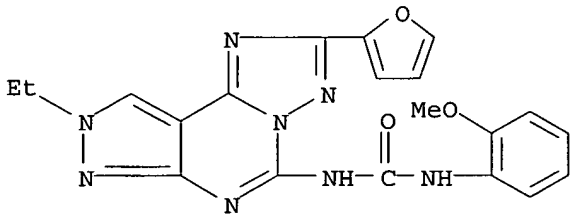
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



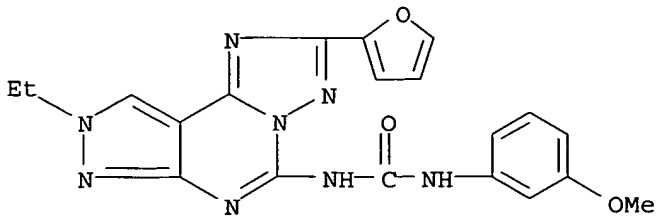
RN 404011-52-5 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



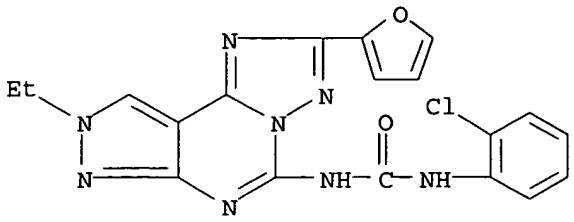
RN 404011-53-6 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



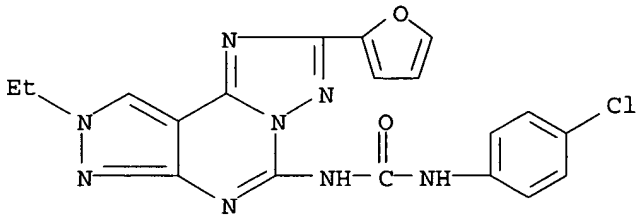
RN 404011-54-7 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



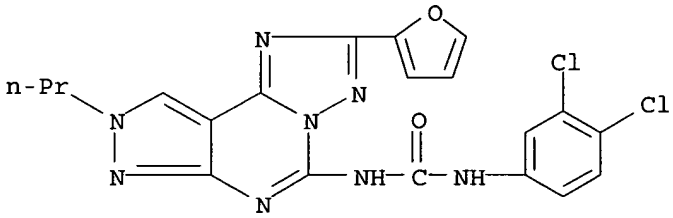
RN 404011-55-8 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



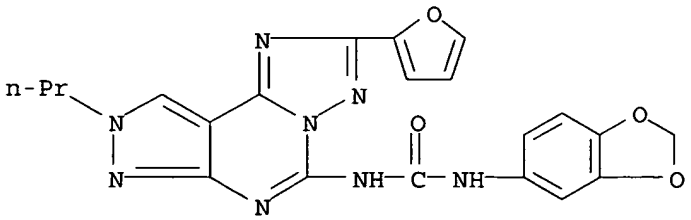
RN 404011-56-9 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



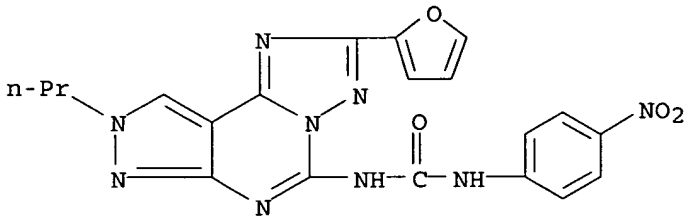
RN 404011-57-0 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



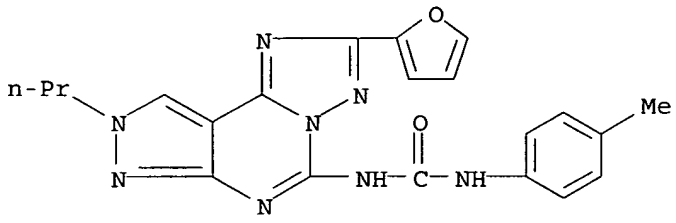
RN 404011-58-1 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



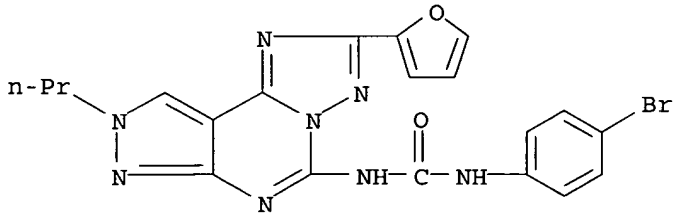
RN 404011-59-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



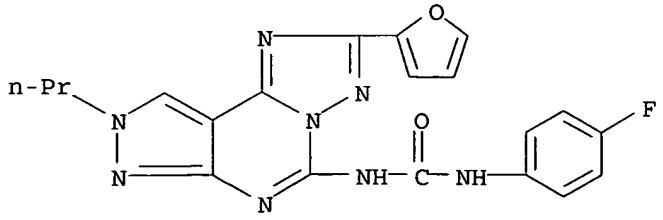
RN 404011-60-5 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



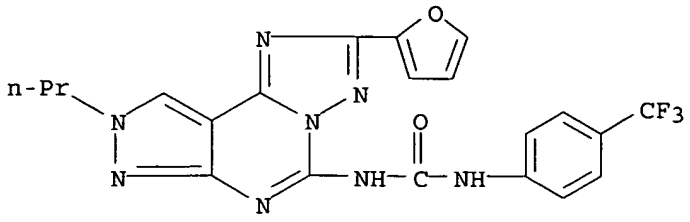
RN 404011-61-6 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



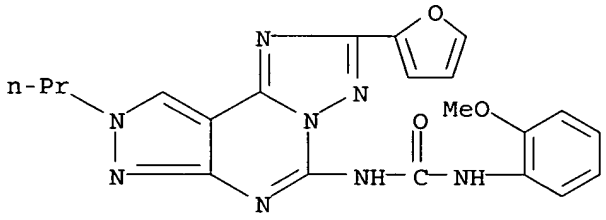
RN 404011-62-7 CAPLUS
CN Urea, N-(4-fluorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



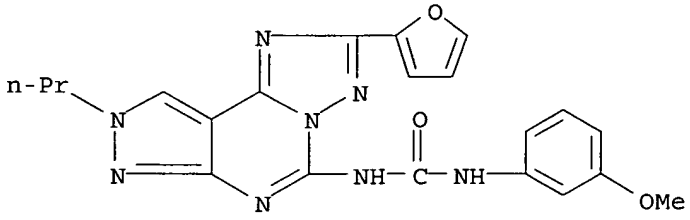
RN 404011-63-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



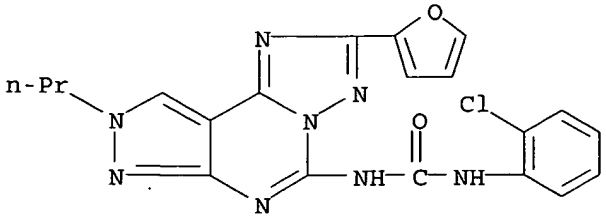
RN 404011-64-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



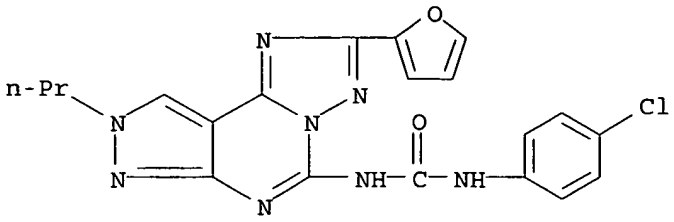
RN 404011-65-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



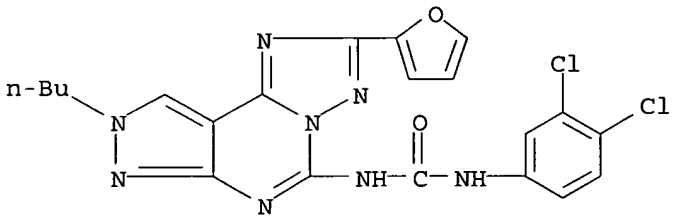
RN 404011-66-1 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



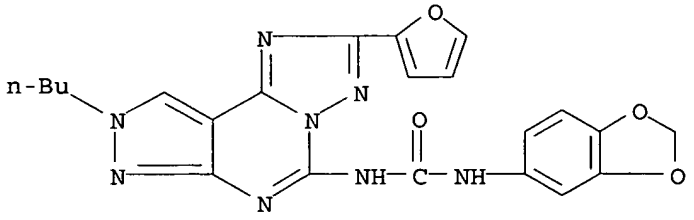
RN 404011-67-2 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



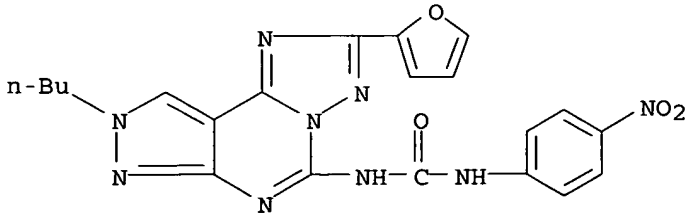
RN 404011-68-3 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



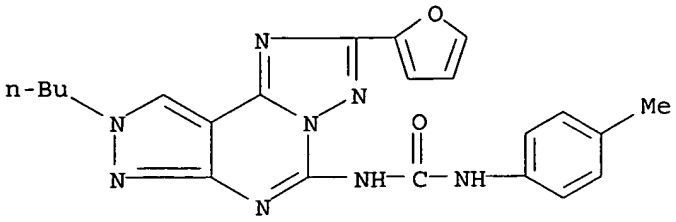
RN 404011-69-4 CAPLUS
CN Urea, N-1,3-benzodioxol-5-yl-N'-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



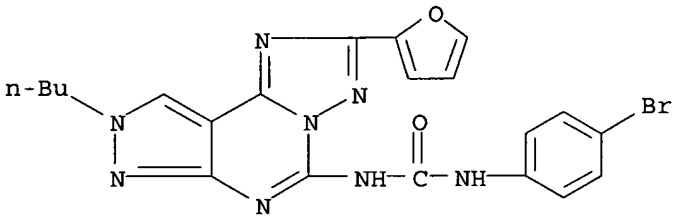
RN 404011-70-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



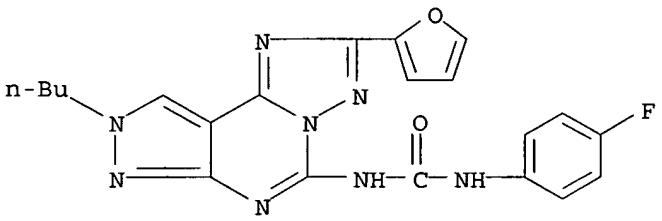
RN 404011-71-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



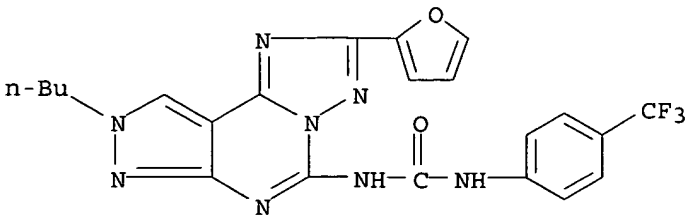
RN 404011-72-9 CAPLUS
CN Urea, N-(4-bromophenyl)-N'-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



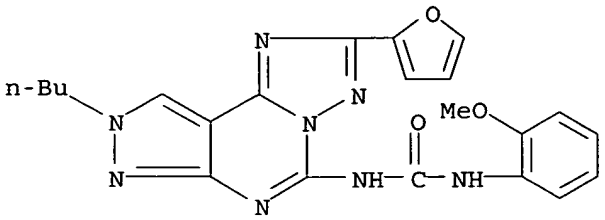
RN 404011-73-0 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



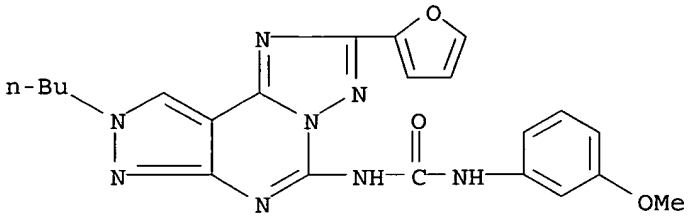
RN 404011-74-1 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



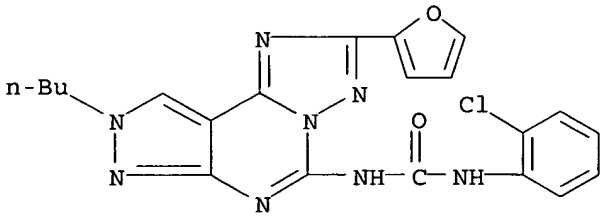
RN 404011-75-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



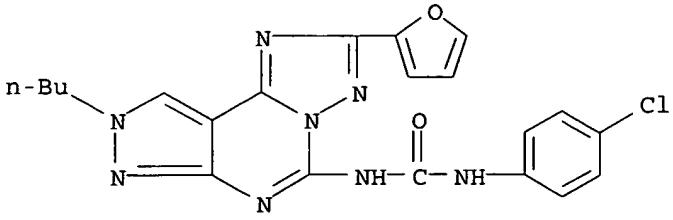
RN 404011-76-3 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



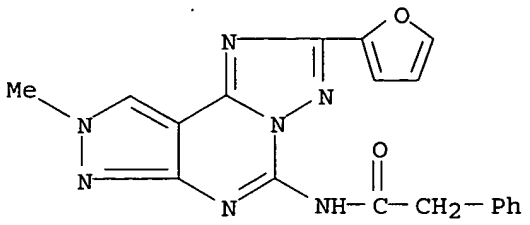
RN 404011-77-4 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(2-chlorophenyl)- (9CI) (CA INDEX NAME)



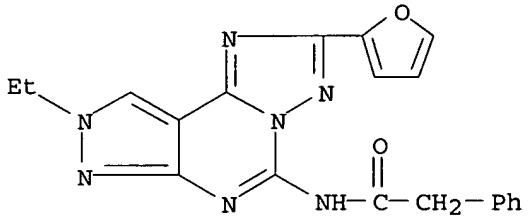
RN 404011-78-5 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



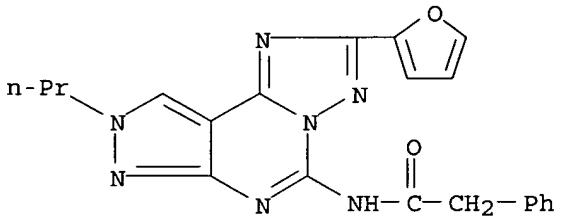
RN 404011-79-6 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



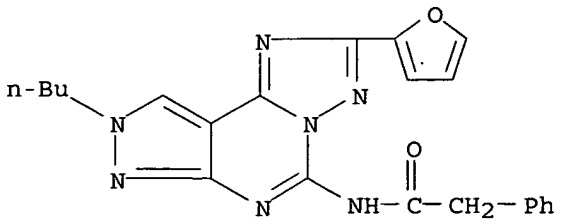
RN 404011-80-9 CAPLUS
CN Benzeneacetamide, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



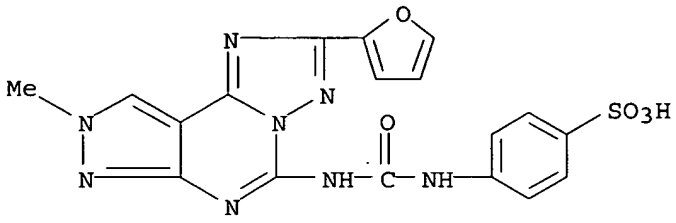
RN 404011-81-0 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



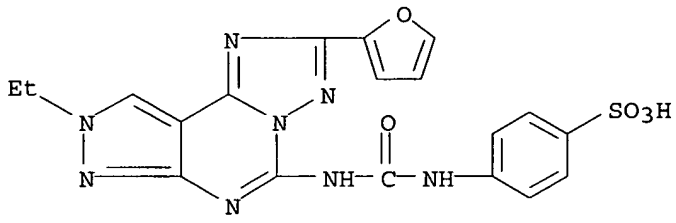
RN 404011-82-1 CAPLUS
CN Benzeneacetamide, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



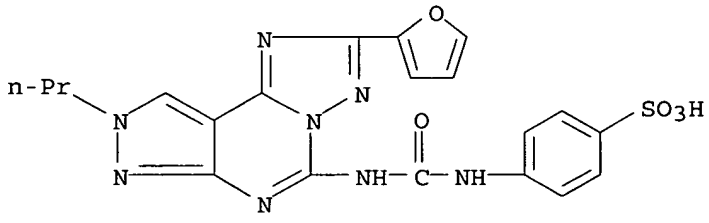
RN 404011-83-2 CAPLUS
CN Benzenesulfonic acid, 4-[[[[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



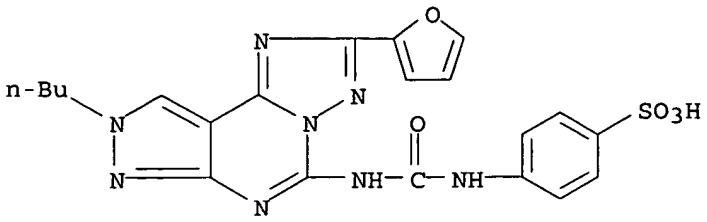
RN 404011-84-3 CAPLUS
CN Benzenesulfonic acid, 4-[[[[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 404011-85-4 CAPLUS
CN Benzenesulfonic acid, 4-[[[[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 404011-86-5 CAPLUS
CN Benzenesulfonic acid, 4-[[[[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

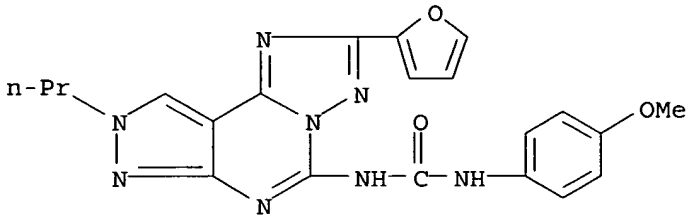
L6 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:879918 CAPLUS
DOCUMENT NUMBER: 136:161304
TITLE: Pharmacological and biochemical characterization of adenosine receptors in the human malignant melanoma A375 cell line
AUTHOR(S): Merighi, Stefania; Varani, Katia; Gessi, Stefania; Cattabriga, Elena; Iannotta, Valeria; Ulouglu, Canan; Leung, Edward; Borea, Pier Andrea
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, Centro Nazionale Di Eccellenza Per Lo Sviluppo Di Metodologie Innovative Per Lo Studio Ed II Trattamento Delle Patologie Infiammatorie, University of Ferrara, Italy
SOURCE: British Journal of Pharmacology (2001), 134(6), 1215-1226
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1 The present work characterizes, from a pharmacol. and biochem. point of view, adenosine receptors in the human malignant melanoma A375 cell line. 2 Adenosine receptors were detected by RT-PCR expts. A1 receptors were characterized using [3H]-DPCPX binding with a KD of 1.9±0.2 nM and Bmax of 23±7 fmol mg-1 of protein. A2A receptors were studied with [3H]-SCH 58261 binding and revealed a KD of 5.1±0.2 nM and a Bmax of 220±7 fmol mg-1 of protein. A3 receptors were studied with the new A3 adenosine receptor antagonist [3H]-MRE 3008F20, the only A3 selective radioligand currently available. Saturation expts. revealed a single high affinity binding site with KD of 3.3±0.7 nM and Bmax of 291±50 fmol mg-1 of protein. 3 The pharmacol. profile of radioligand binding on A375 cells was established using typical adenosine ligands which displayed a rank order of potency typical of the different adenosine receptor subtype. 4 Thermodn. data indicated that radioligand binding to adenosine receptor subtypes in A375 cells was entropy- and enthalpy-driven. 5 In functional assays the high affinity A2A agonists HE-NECA, CGS 21680 and A2A-A2B agonist NECA were able to increase cAMP accumulation in A375 cells whereas A3 agonists Cl-IB-MECA, IB-MECA and NECA were able to stimulate Ca2+ mobilization. 6 In conclusion, all these data indicate, for the first time, that adenosine receptors with a pharmacol. and biochem. profile typical of the A1, A2A, A2B and A3 receptor subtype are present on A375 melanoma cell line.

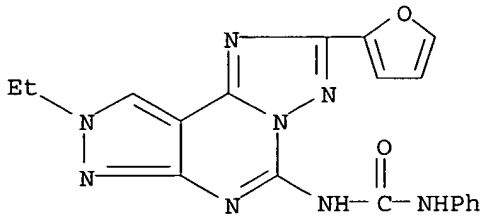
IT **252979-43-4**, MRE 3008F20 **361484-62-0**, MRE 3048F20
361484-63-1, MRE 3055F20 **361484-64-2**, MRE 3062F20
396653-58-0, MRE 3046F20
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(pharmacol. and biochem. characterization of adenosine receptors in human malignant melanoma A375 cell line)

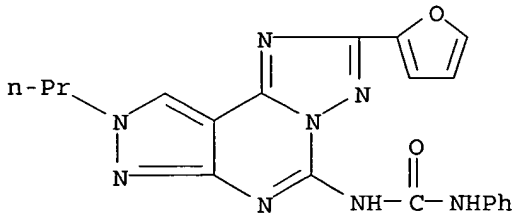
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



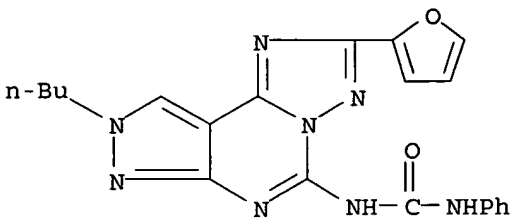
RN 361484-62-0 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



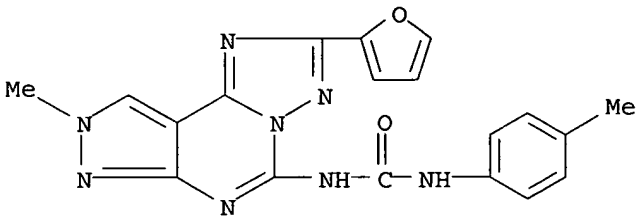
RN 361484-63-1 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



RN 361484-64-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



RN 396653-58-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



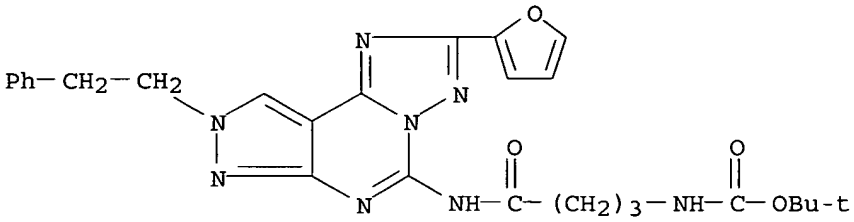
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:714228 CAPLUS
DOCUMENT NUMBER: 136:63590
TITLE: Pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine derivatives as adenosine receptor ligands: a starting point for searching A2B adenosine receptor antagonists
AUTHOR(S): Baraldi, Pier Giovanni; Cacciari, Barbara; Romagnoli, Romeo; Klotz, Karl-Norbert; Spalluto, Giampiero; Varani, Katia; Gessi, Stefania; Merighi, Stefania; Borea, Pier Andrea
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Drug Development Research (2001), 53(2/3), 225-235
CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of novel pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine substituted at N8 pyrazole nitrogen and at the 5-amino group was synthesized and their affinities to all four cloned human adenosine receptor subtypes were evaluated by competition binding assays using [3H]-DPCPX (A1 and A2B), [3H]-SCH 58261 (A2A), and [3H]-MRE3008-F20 (A3) as radioligands. In particular, the structural requirements necessary for adenosine A2B receptor recognition were investigated. These preliminary results confirm that the free amino group at the 5-position confers better A2B affinity, while the effect of the chain at nitrogen pyrazole nucleus, the 8-position, seems to be preferred with respect to the corresponding N7 regioisomers. The introduction of an aminoacyl chain at the 5-amino group produces better selectivity for A2B receptors vs. A2A, but the compds. still remain more potent for A1 and a significant decrease (about 5-fold) of affinity at A2B receptors was observed Surprisingly, with these polar

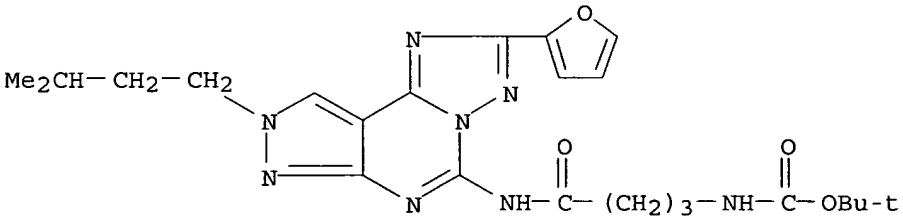
chains a good affinity at human A3 adenosine receptors was also detected. The most interesting compds. in binding studies proved to be potent antagonists (nM range) in functional assays, measuring the inhibition of cAMP production induced by 100 nM NECA.

IT **385441-80-5P 385441-82-7P**
RL: DMA (Drug mechanism of action); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(Pyrazolo[e]1,2,4-triazolo[c]pyrimidine derivs. as adenosine receptor ligands and starting point for searching for A2B adenosine receptor antagonists)

RN 385441-80-5 CAPLUS
CN Carbamic acid, [4-[[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]-4-oxobutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

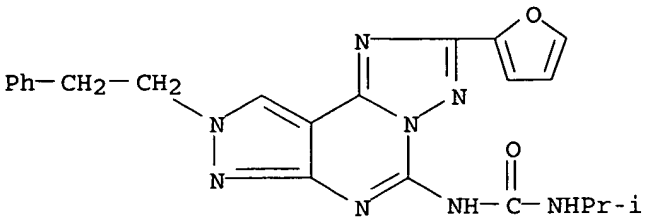


RN 385441-82-7 CAPLUS
CN Carbamic acid, [4-[[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]-4-oxobutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

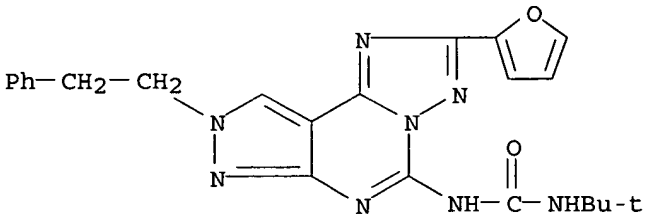


IT **385441-71-4P 385441-72-5P 385441-73-6P**
385441-74-7P 385441-75-8P 385441-76-9P
385441-77-0P 385441-78-1P 385441-79-2P
385441-81-6P 385441-83-8P 385441-84-9P
385441-85-0P 385441-86-1P 385441-87-2P
RL: DMA (Drug mechanism of action); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(Pyrazolo[e]1,2,4-triazolo[c]pyrimidine derivs. as adenosine receptor ligands and starting point for searching for A2B adenosine receptor antagonists)

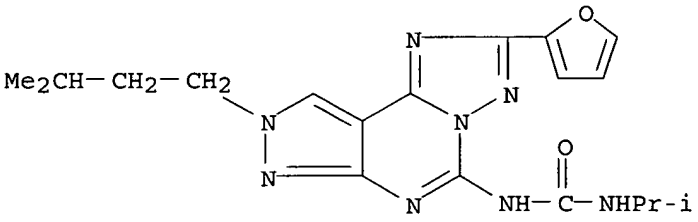
RN 385441-71-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



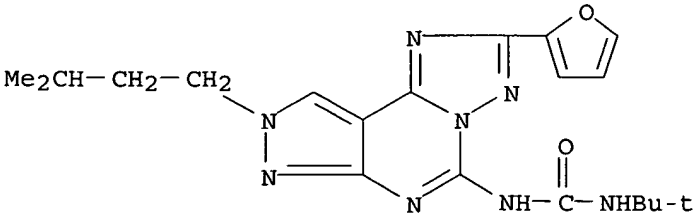
RN 385441-72-5 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 385441-73-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

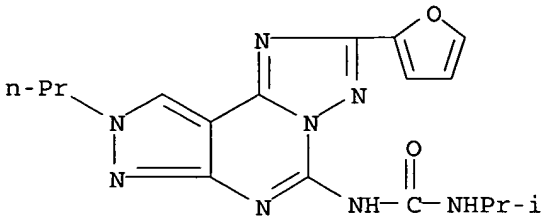


RN 385441-74-7 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

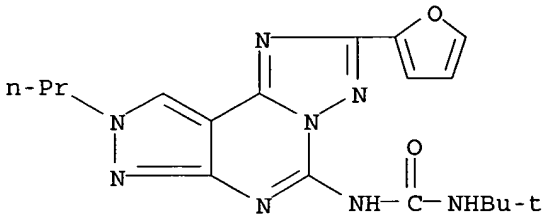


RN 385441-75-8 CAPLUS

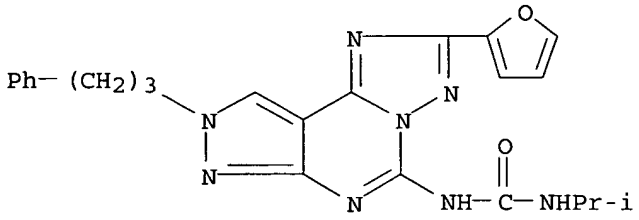
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



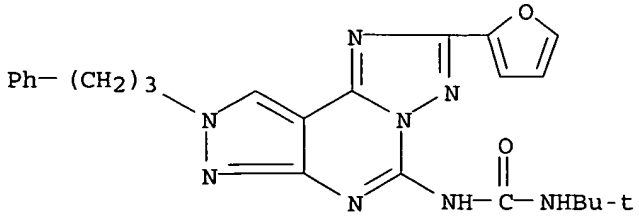
RN 385441-76-9 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



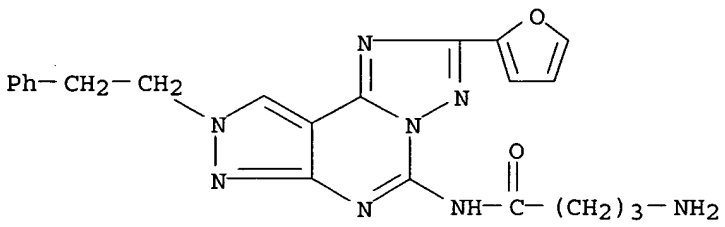
RN 385441-77-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 385441-78-1 CAPLUS
CN Urea, N-(1,1-dimethylethyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

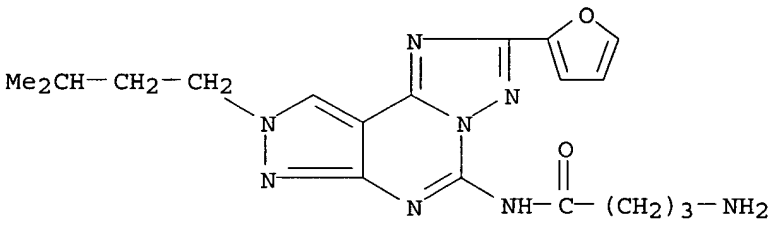


RN 385441-79-2 CAPLUS
CN Butanamide, 4-amino-N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



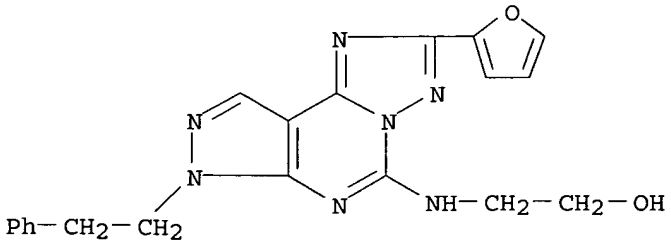
● HCl

RN 385441-81-6 CAPLUS
CN Butanamide, 4-amino-N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

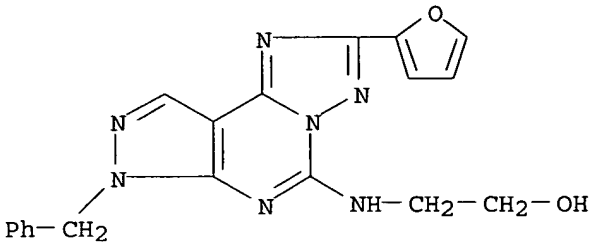


● HCl

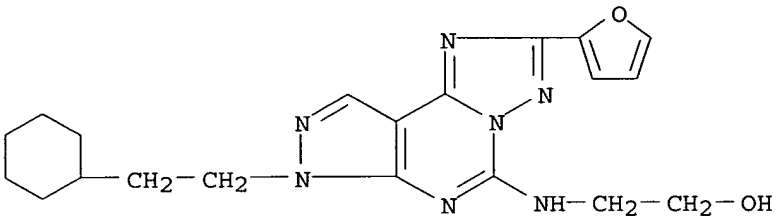
RN 385441-83-8 CAPLUS
CN Ethanol, 2-[[2-(2-furanyl)-7-(2-phenylethyl)-7H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]- (9CI) (CA INDEX NAME)



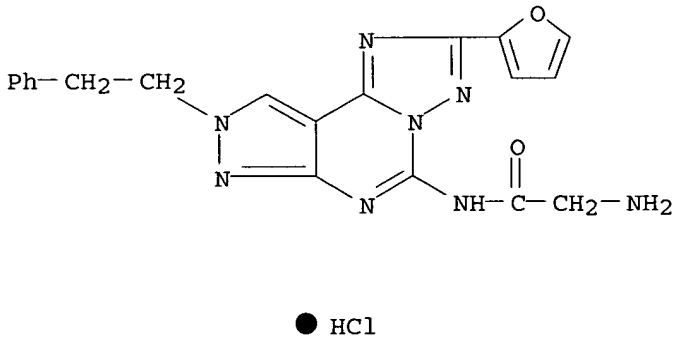
RN 385441-84-9 CAPLUS
CN Ethanol, 2-[[2-(2-furanyl)-7-(phenylmethyl)-7H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]- (9CI) (CA INDEX NAME)



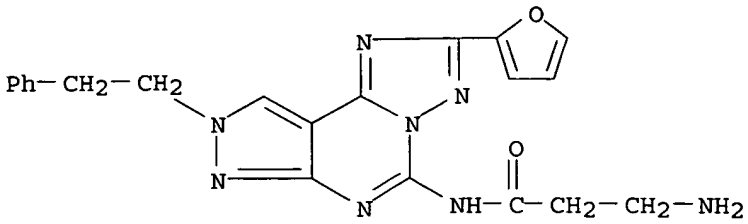
RN 385441-85-0 CAPLUS
CN Ethanol, 2-[[7-(2-cyclohexylethyl)-2-(2-furanyl)-7H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]- (9CI) (CA INDEX NAME)



RN 385441-86-1 CAPLUS
CN Acetamide, 2-amino-N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



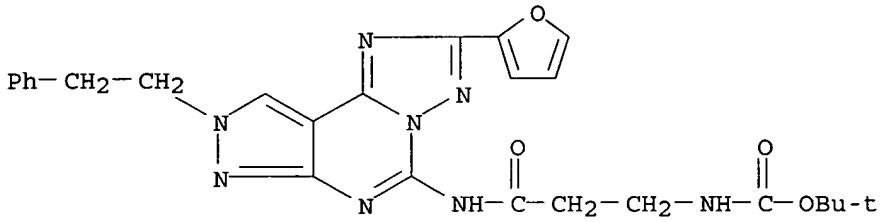
RN 385441-87-2 CAPLUS
CN Propanamide, 3-amino-N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



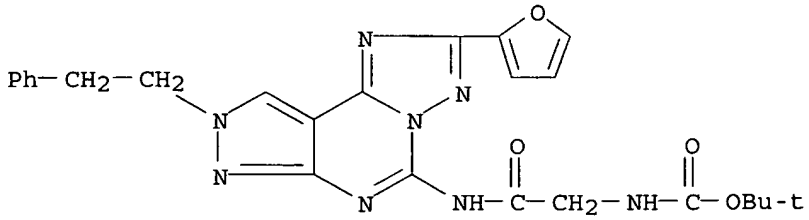
● HCl

IT **385441-88-3P 385441-89-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(Pyrazolo[e]1,2,4-triazolo[c]pyrimidine derivs. as adenosine receptor ligands and starting point for searching for A2B adenosine receptor antagonists)

RN 385441-88-3 CAPLUS
CN Carbamic acid, [3-[[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 385441-89-4 CAPLUS
CN Carbamic acid, [2-[[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:688899 CAPLUS
DOCUMENT NUMBER: 135:339722
TITLE: Pharmacological and biochemical characterization of A3

adenosine receptors in Jurkat T cells

AUTHOR(S): Gessi, Stefania; Varani, Katia; Merighi, Stefania; Morelli, Anna; Ferrari, Davide; Leung, Edward; Baraldi, Pier Giovanni; Spalluto, Giampiero; Borea, Pier Andrea

CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Ferrara, 44100, Italy

SOURCE: British Journal of Pharmacology (2001), 134(1), 116-126
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

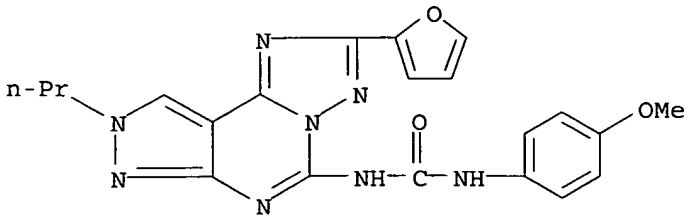
LANGUAGE: English

AB The present work was devoted to the study of A3 adenosine receptors in Jurkat cells, a human leukemia line. The A3 subtype was found by RT-PCR expts. and characterized by using the new A3 adenosine receptor antagonist [3H]-MRE 3008F20, the only A3 selective radioligand currently available. Saturation expts. revealed a single high affinity binding site with KD of 1.9 nM and Bmax of 1.3 pmol mg-1 of protein. The pharmacol. profile of [3H]-MRE 3008F20 binding on Jurkat cells was established using typical adenosine ligands which displayed a rank order of potency typical of the A3 subtype. Thermodn. data indicated that [3H]-MRE 3008F20 binding to A3 subtype in Jurkat cells was entropy- and enthalpy-driven, according with that found in cells expressing the recombinant human A3 subtype. In functional assays the high affinity A3 agonists Cl-IB-MECA and IB-MECA were able to inhibit cAMP accumulation and stimulate Ca2+ release from intracellular Ca2+ pools followed by Ca2+ influx. The presence of the other adenosine subtypes was investigated in Jurkat cells. A1 receptors were characterized using [3H]-DPCPX binding with a KD of 0.9 nM and Bmax of 42 fmol mg-1 of protein. A2A receptors were studied with [3H]-SCH 58261 binding and revealed a KD of 2.5 nM and a Bmax of 1.4 pmol mg-1 of protein. In conclusion, by the first antagonist radioligand [3H]-MRE 3008F20 the authors could demonstrate the existence of functional A3 receptors on Jurkat cells.

IT **252979-43-4**, MRE 3008F20
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(A3 adenosine receptor antagonist; pharmacol., thermodn. and biochem. characterization of A3 adenosine receptors in Jurkat T cells)

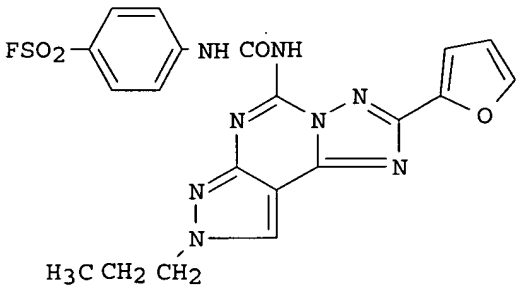
RN 252979-43-4 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:514232 CAPLUS
DOCUMENT NUMBER: 135:251425
TITLE: Fluorosulfonyl- and bis-(β-chloroethyl)amino-phenylamino functionalized pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine derivatives: irreversible antagonists at the human A3 adenosine receptor and molecular modeling studies
AUTHOR(S): Baraldi, Pier Giovanni; Cacciari, Barbara; Moro, Stefano; Romagnoli, Romeo; Ji, Xiao-duo; Jacobson, Kenneth A.; Gessi, Stefania; Borea, Pier Andrea; Spalluto, Giampiero
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Journal of Medicinal Chemistry (2001), 44(17), 2735-2742
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



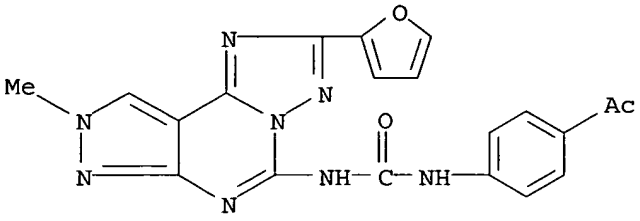
I

AB A series of pyrazolotriazolopyrimidines was previously reported to be highly potent and selective human A3 adenosine receptor antagonists (Baraldi et al. J. Med. Chemical 2000, 43, 4768-4780). A derivative having a Me group at the N8 pyrazole combined with a 4-methoxyphenylcarbamoyl moiety at N5 position, displayed a Ki value at the hA3 receptor of 0.2 nM. We now describe chemical reactive derivs. which act as irreversible inhibitors of this receptor. Electrophilic groups, specifically sulfonyl fluoride and nitrogen mustard (bis-(β-chloroethyl)amino) moieties, have been incorporated at the 4-position of the aryl urea group. Membranes containing the recombinant hA3 receptor were preincubated with the compds. and washed exhaustively. The loss of ability to bind radioligand following this treatment indicated irreversible binding. The most potent compound in irreversibly binding to the receptor was I, which contained a sulfonyl fluoride moiety and a Pr group at the N8 pyrazole nitrogen. The bis-(β-chloroethyl)amino derivs. displayed a much smaller degree of irreversible binding than the sulfonyl fluoride derivs. A computer-generated model of the human A3 receptor was built and analyzed to help interpret these results. The model of the A3 transmembrane region was derived using primary sequence comparison, secondary structure predictions, and three-dimensional homol. building, using the recently published crystal structure of rhodopsin as a template. According to our model, sulfonyl fluoride derivs. could dock within the hypothetical TM

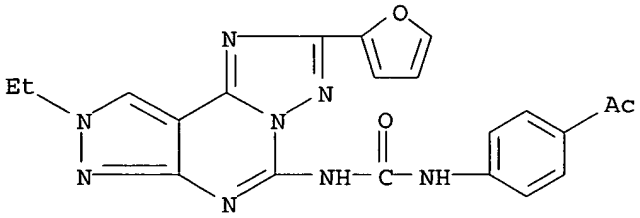
binding domain, adopting two different energetically favorable conformations. We have identified two amino acids, Ser247 and Cys251, both in TM6, as potential nucleophilic partners of the irreversible binding to the receptor.

IT **361484-49-3 361484-50-6 361484-51-7 361484-52-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(fluorosulfonyl- and chloroethylamino-phenylamino functionalized pyrazolotriazolopyrimidines as irreversible antagonists of human A3 adenosine receptor)

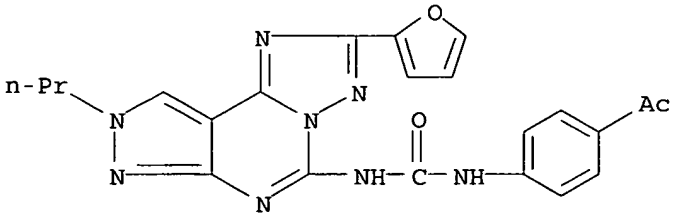
RN 361484-49-3 CAPLUS
CN Urea, N-(4-acetylphenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



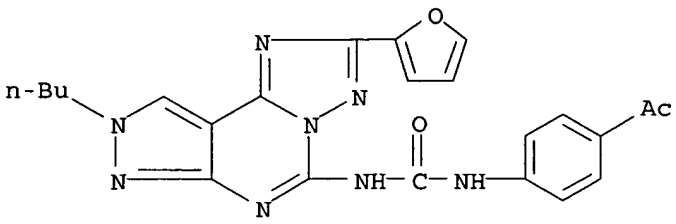
RN 361484-50-6 CAPLUS
CN Urea, N-(4-acetylphenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 361484-51-7 CAPLUS
CN Urea, N-(4-acetylphenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

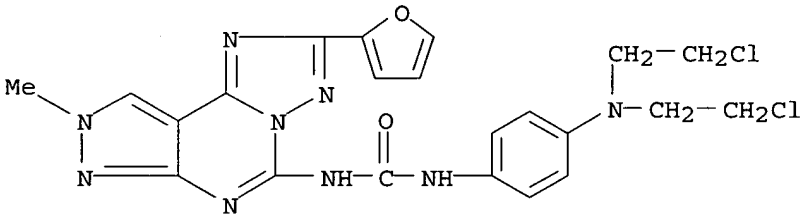


RN 361484-52-8 CAPLUS
CN Urea, N-(4-acetylphenyl)-N'-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

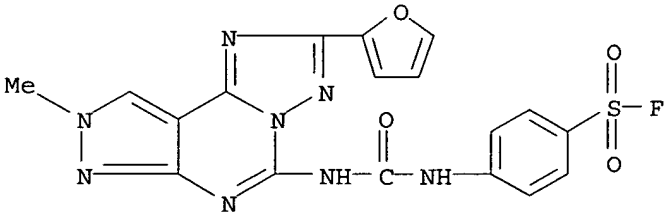


IT **361484-53-9P 361484-54-0P 361484-55-1P**
361484-56-2P 361484-57-3P 361484-58-4P
361484-59-5P 361484-60-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(fluorosulfonyl- and chloroethylamino-phenylamino functionalized pyrazolotriazolopyrimidines as irreversible antagonists of human A3 adenosine receptor)

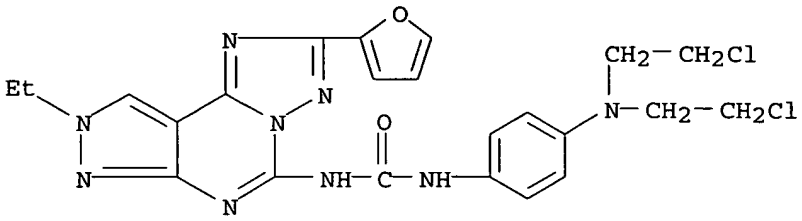
RN 361484-53-9 CAPLUS
CN Urea, N-[4-[bis(2-chloroethyl)amino]phenyl]-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



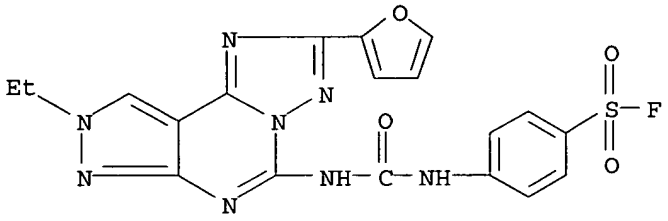
RN 361484-54-0 CAPLUS
CN Benzenesulfonyl fluoride, 4-[[[[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



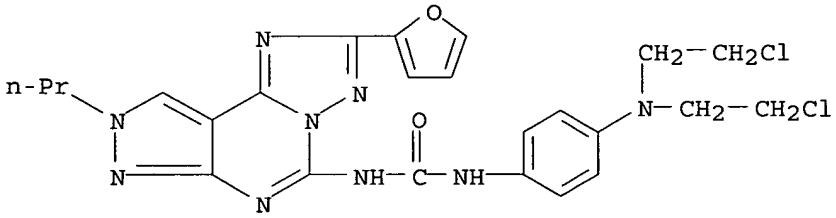
RN 361484-55-1 CAPLUS
CN Urea, N-[4-[bis(2-chloroethyl)amino]phenyl]-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



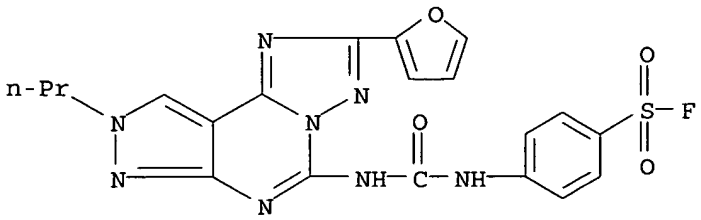
RN 361484-56-2 CAPLUS
CN Benzenesulfonyl fluoride, 4-[[[[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 361484-57-3 CAPLUS
CN Urea, N-[4-[bis(2-chloroethyl)amino]phenyl]-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

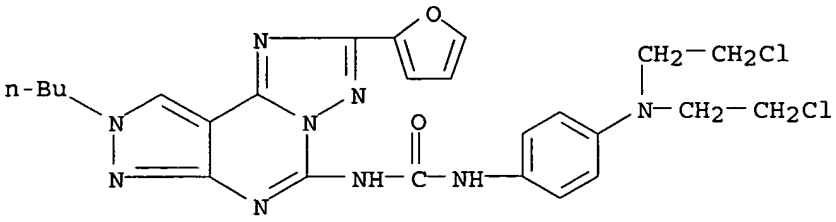


RN 361484-58-4 CAPLUS
CN Benzenesulfonyl fluoride, 4-[[[[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

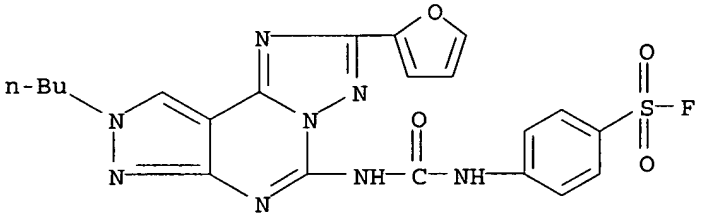


RN 361484-59-5 CAPLUS

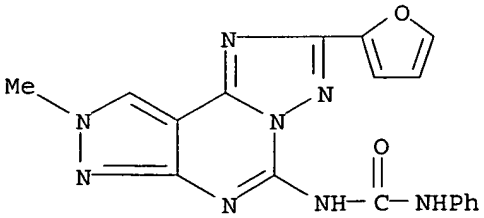
CN Urea, N-[4-[bis(2-chloroethyl)amino]phenyl]-N'-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



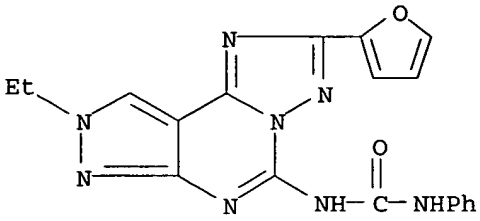
RN 361484-60-8 CAPLUS
CN Benzenesulfonyl fluoride, 4-[[[[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



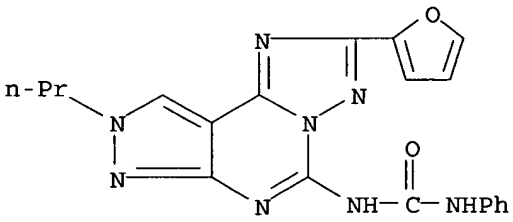
IT **361484-61-9P 361484-62-0P 361484-63-1P**
361484-64-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(fluorosulfonyl- and chloroethylamino-phenylamino functionalized pyrazolotriazolopyrimidines as irreversible antagonists of human A3 adenosine receptor)
RN 361484-61-9 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



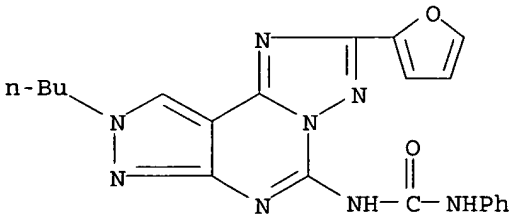
RN 361484-62-0 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



RN 361484-63-1 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



RN 361484-64-2 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

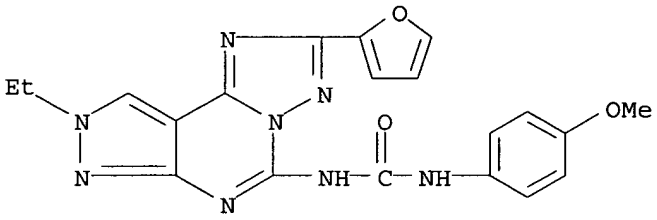
L6 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:342062 CAPLUS
DOCUMENT NUMBER: 135:146779
TITLE: Pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine derivatives: a new pharmacological tool for the characterization of the human A3 adenosine receptor
AUTHOR(S): Baraldi, Pier Giovanni; Cacciari, Barbara; Romagnoli, Romeo; Spalluto, Giampiero; Varani, Katia; Gessi, Stefania; Merighi, Stefania; Borea, Pier Andrea
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Drug Development Research (2001), 52(1/2), 406-415
CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adenosine regulates many physiol. functions by interaction with four different G-protein-coupled receptors classified as A1, A2A, A2B, and A3. While adenosine A1 and A2A receptor subtypes have been pharmacol. characterized through the use of selective ligands, the A2B and A3 adenosine receptor subtypes are presently under study to better understand their physio-pathol. functions. In particular, activation of adenosine A3 receptors has been shown to stimulate phospholipase C and D and to inhibit adenylate cyclase. Activation of A3 adenosine receptors also causes the release of inflammatory mediators such as histamine from mast cells, which are responsible for processes such as inflammation and hypotension. For these reasons, it has been suggested that A3 adenosine receptor antagonists can be considered potential drugs for the treatment of asthma and inflammation. In the last few years different classes of heterocyclic compds. have been identified as A3 adenosine antagonists, but none of the tested compds. showed significant selectivity for A3 adenosine receptor subtype. Herein, we report our recent results on a class of pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine derivs. as a new class of potent and selective human A3 adenosine receptor antagonists. The full characterization of the first high-affinity radioligand antagonist for this receptor subtype, designated [3H] MRE3008F20, is briefly summarized.

IT **252979-41-2 252979-42-3 252979-43-4,**
MRE3008F20 **252979-44-5 252979-45-6 252979-46-7**
252979-47-8 252979-48-9
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pyrazolopyrimidine derivs. as new pharmacol. tools for characterization of human A3 adenosine receptor)

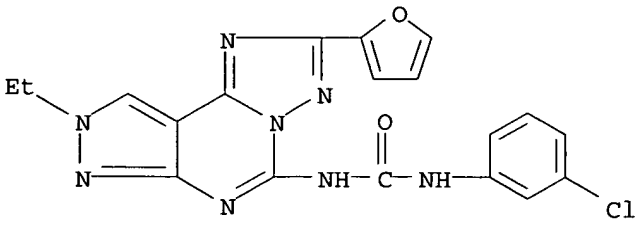
RN 252979-41-2 CAPLUS

CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 252979-42-3 CAPLUS

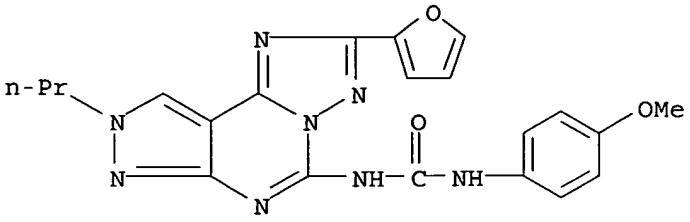
CN Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



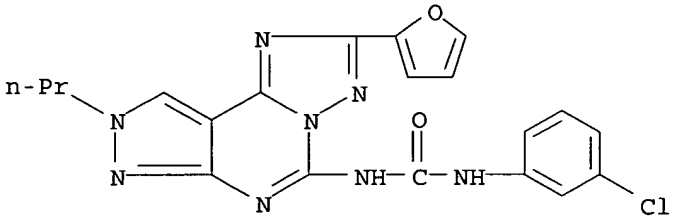
RN 252979-43-4 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-

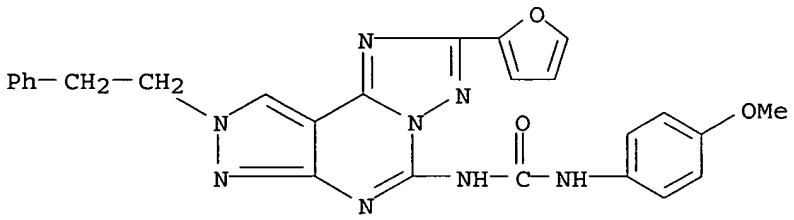
c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



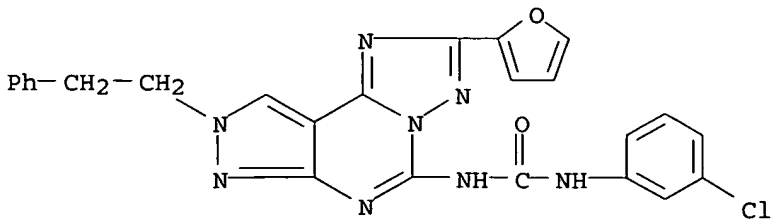
RN 252979-44-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



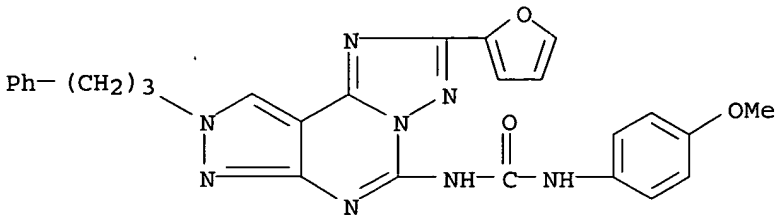
RN 252979-45-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



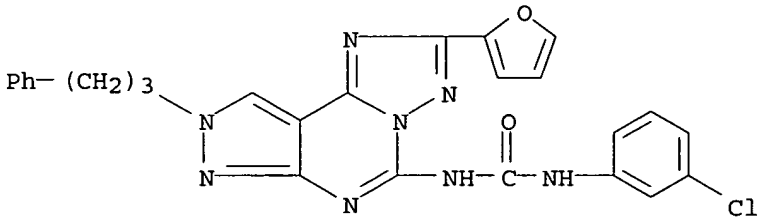
RN 252979-46-7 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 252979-47-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



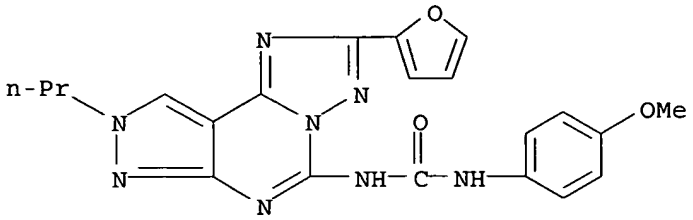
RN 252979-48-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:891037 CAPLUS
DOCUMENT NUMBER: 134:247274
TITLE: New potent and selective human adenosine A3 receptor antagonists
AUTHOR(S): Baraldi, P. G.; Borea, P. A.
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Trends in Pharmacological Sciences (2000), 21(12), 456-459
CODEN: TPHSDY; ISSN: 0165-6147
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 25 refs., describing evaluation of pathophysiol. role of human adenosine A3 receptors by subtype-selective agonists and antagonists, design of selective A3 receptor ligands (mainly antagonists), and preparation of a selective high-affinity radiolabeled compound ([3H]MRE 3008F20).
IT **252979-43-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potent and selective human adenosine A3 receptor antagonists)

RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



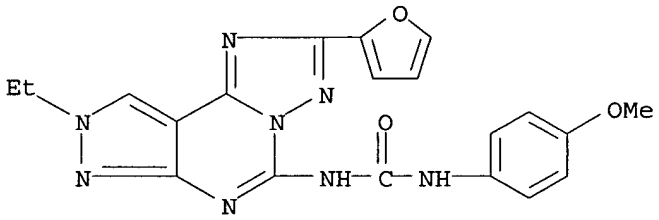
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:818494 CAPLUS
DOCUMENT NUMBER: 134:131485
TITLE: Pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine Derivatives as Highly Potent and Selective Human A3 Adenosine Receptor Antagonists: Influence of the Chain at the N8 Pyrazole Nitrogen
AUTHOR(S): Baraldi, Pier Giovanni; Cacciari, Barbara; Romagnoli, Romeo; Spalluto, Giampiero; Moro, Stefano; Klotz, Karl-Norbert; Leung, Edward; Varani, Katia; Gessi, Stefania; Merighi, Stefania; Borea, Pier Andrea
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche and Dipartimento di Medicina Clinica e Sperimentale-Sezione di Farmacologia, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Journal of Medicinal Chemistry (2000), 43(25), 4768-4780
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An enlarged series of pyrazolotriazolopyrimidines previously reported, in preliminary form (Baraldi et al. J. Med. Chemical 1999, 42, 4473-4478), as highly potent and selective human A3 adenosine receptor antagonists is described. The synthesized compds. showed A3 adenosine receptor affinity in the sub-nanomolar range and high levels of selectivity evaluated in radioligand binding assays at human A1, A2A, A2B, and A3 adenosine receptors. In particular, the effect of the chain at the N8 pyrazole nitrogen was analyzed. This study allowed us to identify the derivative with the Me group at the N8 pyrazole combined with the 4-methoxyphenylcarbamoyl moiety at the N5 position as the compound with the best binding profile in terms of both affinity and selectivity (hA3 = 0.2 nM, hA1/hA3 = 5485, hA2A/hA3 = 6950, hA2B/hA3 = 1305). All the compds. proved to be full antagonists in a specific functional model where the inhibition of cAMP generation by IB-MECA was measured in membranes of CHO cells stably transfected with the human A3 receptor. The new compds. are among the most potent and selective A3 antagonists so far described. The derivs. with higher affinity at human A3 adenosine receptors proved to be antagonists, in the cAMP assay, capable of inhibiting the effect of IB-MECA with IC50 values in the nanomolar range, with a trend strictly similar to that observed in the binding assay. Also a mol. modeling study

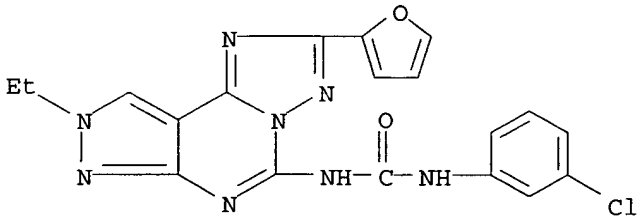
was carried out, with the aim to identify possible pharmacophore maps. In fact, a sterically controlled structure-activity relationship was found for the N8 pyrazole substituted derivs., showing a correlation between the calculated mol. volume of pyrazolo[4,3-e]1,2,4-triazolo[1,5-c]pyrimidine derivs.
and their exptl. Ki values.

IT **252979-41-2P 252979-42-3P 252979-43-4P**
252979-44-5P 252979-45-6P 252979-46-7P
252979-47-8P 252979-48-9P 261629-22-5P
261629-23-6P 261629-24-7P 261629-25-8P
261629-26-9P 261629-27-0P 261629-28-1P
261629-29-2P 264623-54-3P 321661-16-9P
321661-18-1P 321661-27-2P 321661-29-4P
321661-35-2P 321661-36-3P 321661-37-4P
321661-38-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidine derivs. and their activity as A3 adenosine receptor antagonists)

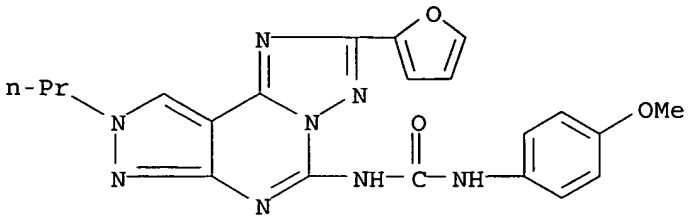
RN 252979-41-2 CAPLUS
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



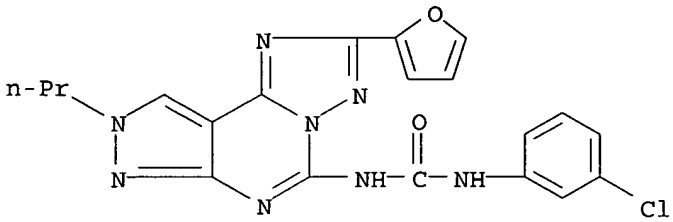
RN 252979-42-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



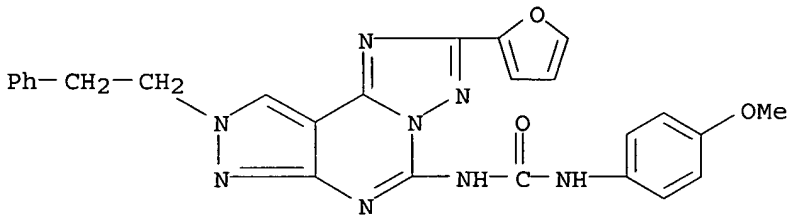
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



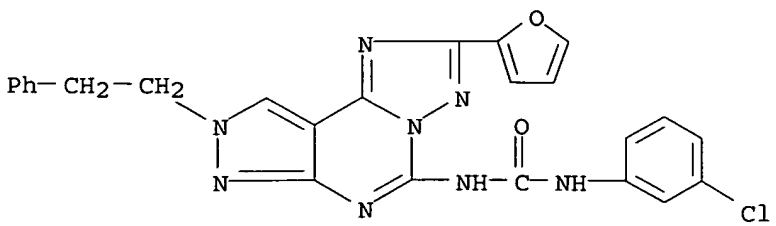
RN 252979-44-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 252979-45-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

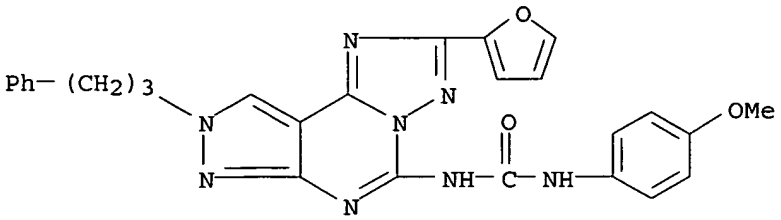


RN 252979-46-7 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

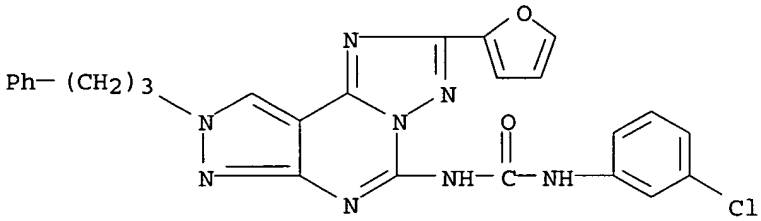


RN 252979-47-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-

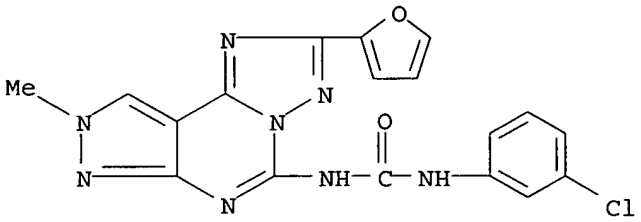
e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



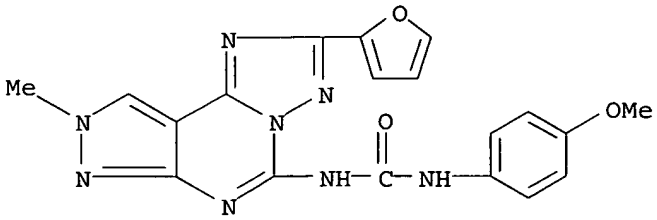
RN 252979-48-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



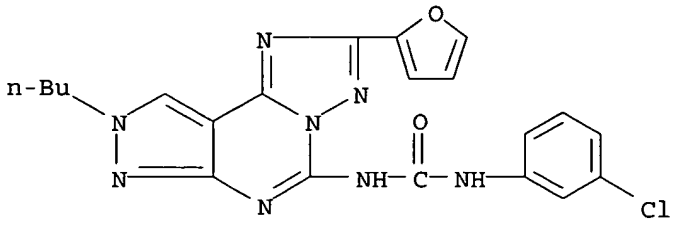
RN 261629-22-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



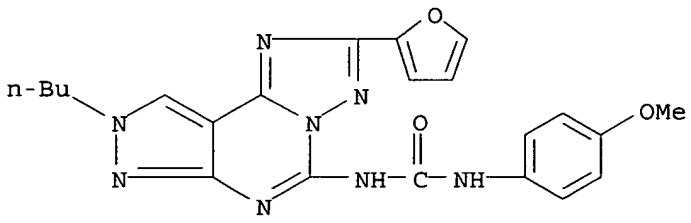
RN 261629-23-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



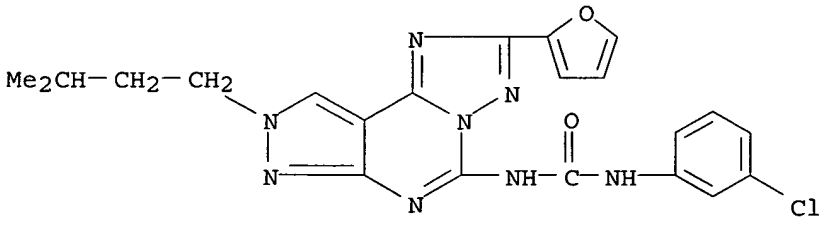
RN 261629-24-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



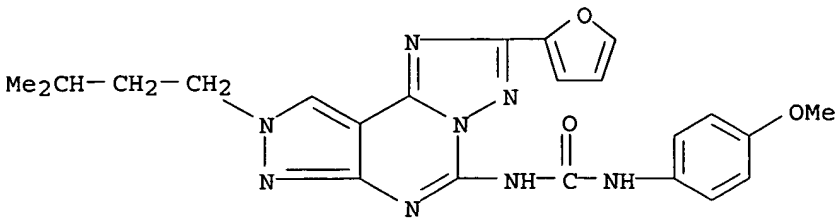
RN 261629-25-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



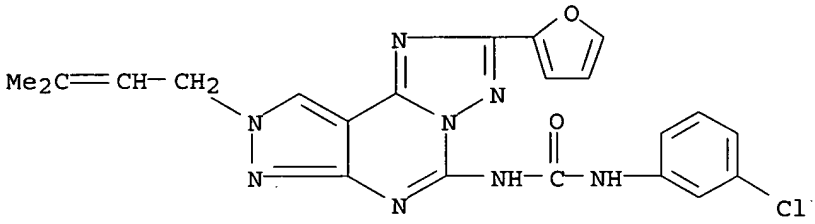
RN 261629-26-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



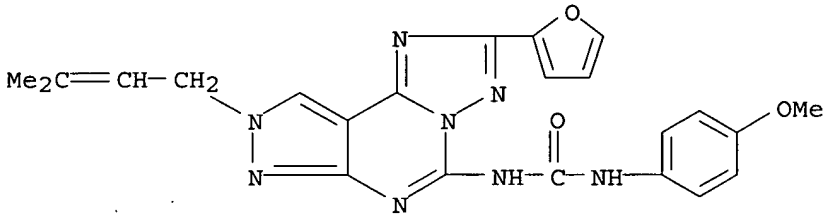
RN 261629-27-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



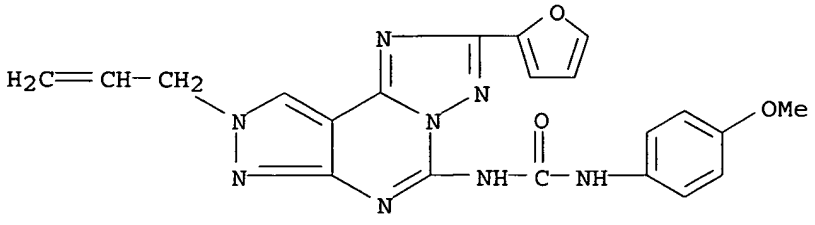
RN 261629-28-1 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 261629-29-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

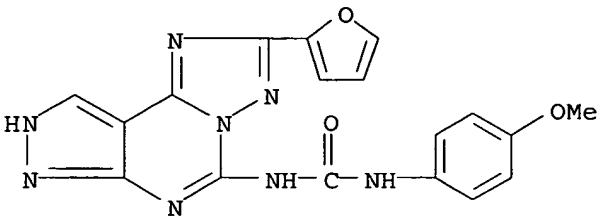


RN 264623-54-3 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-propenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

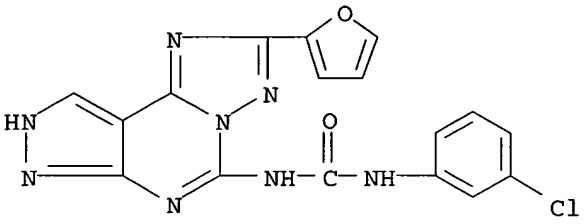


RN 321661-16-9 CAPLUS

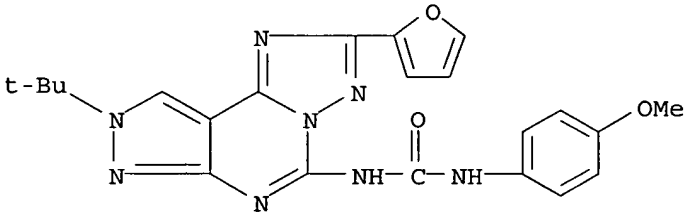
CN Urea, N-[2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



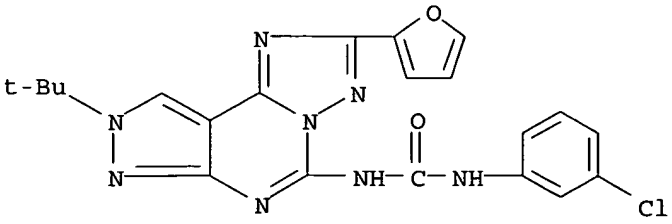
RN 321661-18-1 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



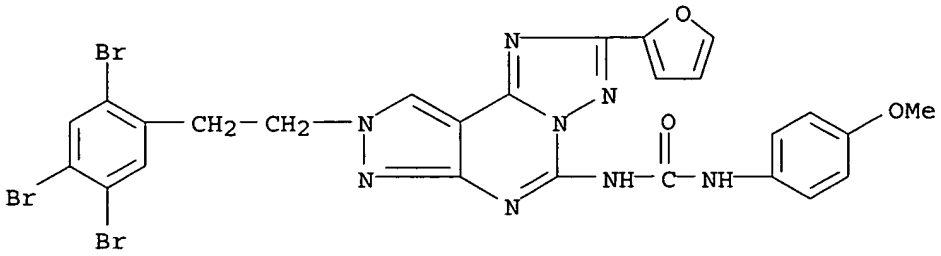
RN 321661-27-2 CAPLUS
CN Urea, N-[8-(1,1-dimethylethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



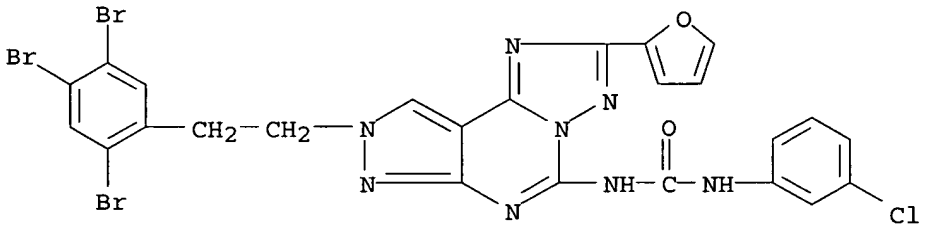
RN 321661-29-4 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-(1,1-dimethylethyl)-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 321661-35-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-[2-(2,4,5-tribromophenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

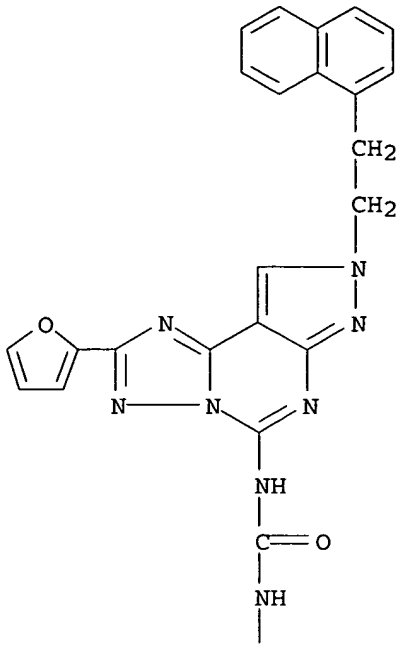


RN 321661-36-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-[2-(2,4,5-tribromophenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

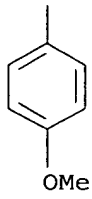


RN 321661-37-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-[2-(1-naphthalenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

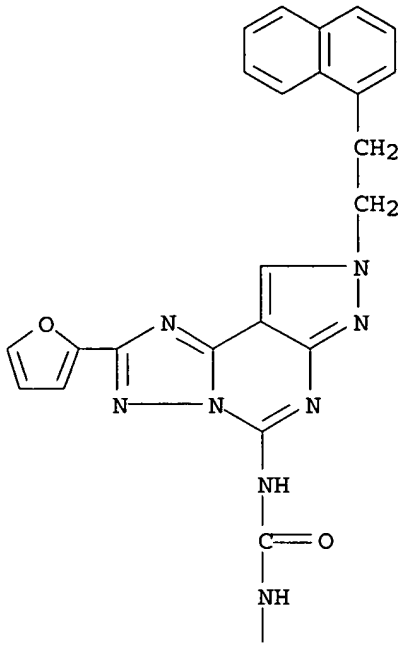


PAGE 2-A

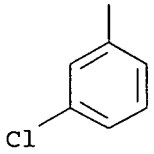


RN 321661-38-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-[2-(1-naphthalenyl)ethyl]-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:303389 CAPLUS
DOCUMENT NUMBER: 133:38565
TITLE: [3H]MRE 3008F20: a novel antagonist radioligand for the pharmacological and biochemical characterization of human A3 adenosine receptors
AUTHOR(S): Varani, Katia; Merighi, Stefania; Gessi, Stefania; Klotz, Karl-Norbert; Lfung, Edward; Baraldi, Pier Giovanni; Cacciari, Barbara; Romagnoli, Romeo; Spalluto, Giampiero; Borfa, Pier Andrea
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Pharmacology Unit, University of Ferrara, Italy
SOURCE: Molecular Pharmacology (2000), 57(5), 968-975
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal

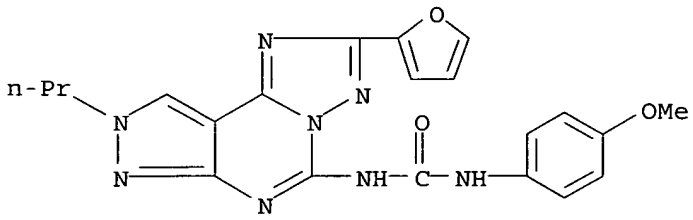
LANGUAGE: English

AB The lack of a radiolabeled selective A3 adenosine receptor antagonist is a major drawback for an adequate characterization of this receptor subtype. This paper describes the pharmacol. and biochem. characterization of the tritiated form of a new potent A3 adenosine receptor antagonist, the pyrazolo triazolo pyrimidine derivative [3H]5N-(4-methoxyphenylcarbamoyl)amino-8-propyl-2-(2-furyl)pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine ([3H]MRE 3008F20). [3H]MRE 3008F20 bound specifically to the human adenosine A3 receptor expressed in CHO cells (hA3CHO), and saturation anal. revealed a single high affinity binding site, KD = 0.80 nM, with a Bmax = 300 fmol/mg protein. This new ligand displayed high selectivity (1294-, 165-, and 2471-fold) in binding assay to human A3 vs. A1, A2A, and A2B receptors, resp., and binds to the rat A3 receptors with a Ki >10 μM. The pharmacol. profile of [3H]MRE 3008F20 binding to hA3CHO cells was evaluated using known adenosine receptor agonists and antagonists with a rank order of potency consistent with that typically found for interactions with the A3 adenosine receptors. In the adenylyl cyclase assay the same compds. exhibited a rank order of potency identical with that observed in binding expts. Thermodn. data indicated that [3H]MRE 3008F20 binding to hA3CHO is entropy- and enthalpy-driven in agreement with the typical behavior of other adenosine antagonists to A1 and A2A receptors. These results show that [3H]MRE 3008F20 is the first antagonist radioligand with high affinity and selectivity for the human A3 adenosine receptor and may be used to investigate the physiopathol. role of A3 adenosine receptors.

IT **252979-43-4**, MRE 3008F20
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(MRE 3008F20 as antagonist ligand for pharmacol. and biochem. characterization of human A3 adenosine receptors)

RN 252979-43-4 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:190930 CAPLUS

DOCUMENT NUMBER: 132:217158

TITLE: 1,2,4-Triazolo[1,5-c]pyrimidine adenosine A3 receptor modulators, preparation thereof, and therapeutic and diagnostic use

INVENTOR(S): Baraldi, Pier Giovanni; Borea, Pier Andrea

PATENT ASSIGNEE(S): Medco Research Inc., USA

SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015231	A1	20000323	WO 1999-US21103	19990915
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6448253	B1	20020910	US 1998-154435	19980916
US 6407236	B1	20020618	US 1999-379300	19990823
CA 2332007	AA	20000323	CA 1999-2332007	19990915
AU 9962482	A1	20000403	AU 1999-62482	19990915
AU 749211	B2	20020620		
GB 2353527	A1	20010228	GB 2000-27879	19990915
GB 2353527	B2	20040225		
BR 9913766	A	20010605	BR 1999-13766	19990915
DE 19983530	T	20011108	DE 1999-19983530	19990915
JP 2002524519	T2	20020806	JP 2000-569815	19990915
NZ 509149	A	20030829	NZ 1999-509149	19990915
RU 2250904	C2	20050427	RU 2000-127721	19990915
SE 2000003984	A	20001222	SE 2000-3984	20001101
SE 522578	C2	20040217		
NO 2000005508	A	20010315	NO 2000-5508	20001101
NO 318078	B1	20050131		
LU 90687	A1	20001219	LU 2000-90687	20001206
HK 1035671	A1	20050218	HK 2001-106364	20010907
PRIORITY APPLN. INFO.:			US 1998-154435 A	19980916
			US 1999-379300 A	19990823
			WO 1999-US21103 W	19990915

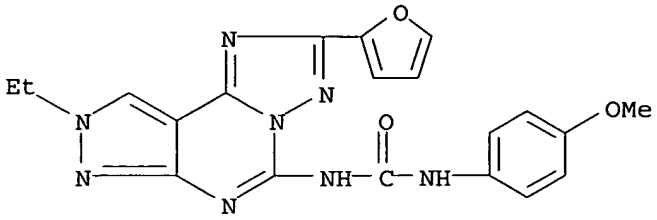
OTHER SOURCE(S): MARPAT 132:217158

AB The title compds. (Markush included), which have selective A3 adenosine receptor agonist activity, are provided. These compds. can be used in a pharmaceutical composition to treat disorders caused by excessive activation of the A3 receptor, or can be used in a diagnostic application to determine the relative binding of other compds. to the A3 receptor. The compds. can be labeled, for example with fluorescent or radiolabels, and the labels used in vivo or in vitro to determine the presence of tumor cells which possess a high concentration of adenosine A3 receptors.

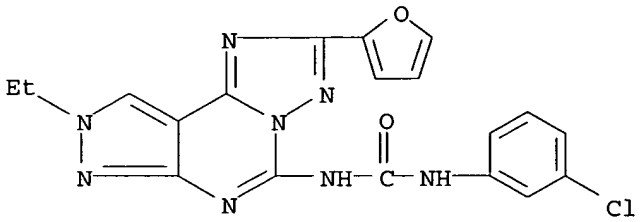
IT **252979-41-2P 252979-42-3P 252979-43-4P**
252979-44-5P 252979-45-6P 252979-46-7P
252979-47-8P 252979-48-9P 261629-22-5P
261629-23-6P 261629-24-7P 261629-25-8P
261629-26-9P 261629-27-0P 261629-28-1P
261629-29-2P 261629-30-5P 261629-31-6P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(triazolopyrimidine adenosine A3 receptor modulator preparation and therapeutic and diagnostic use)

RN 252979-41-2 CAPLUS

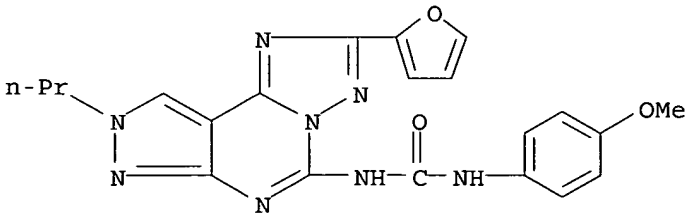
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



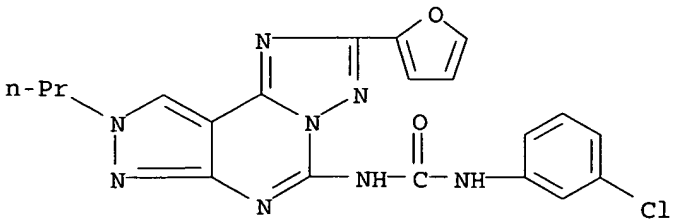
RN 252979-42-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



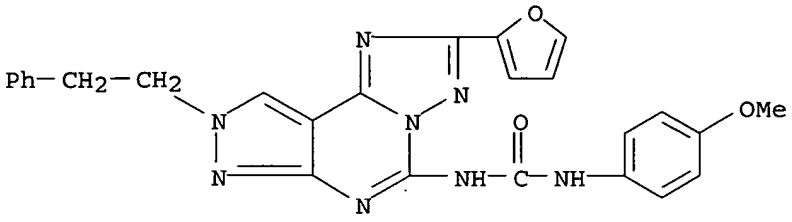
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



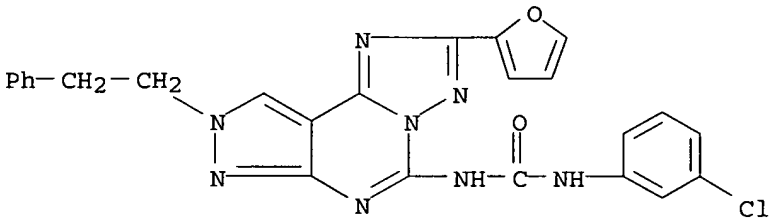
RN 252979-44-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



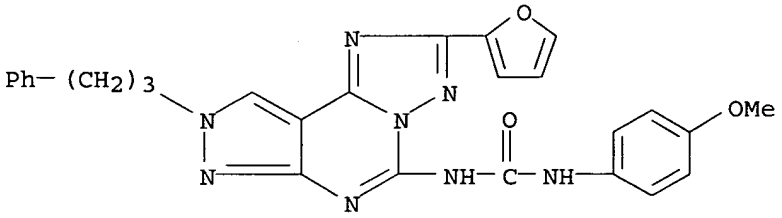
RN 252979-45-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



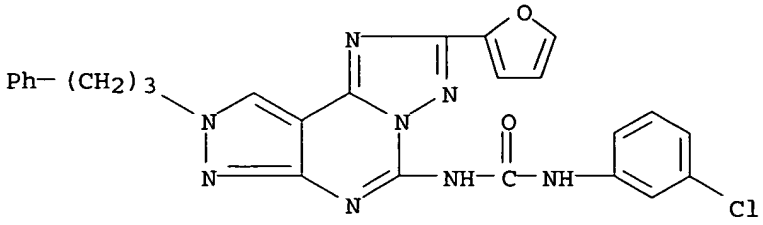
RN 252979-46-7 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



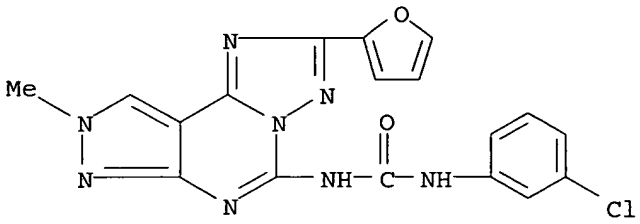
RN 252979-47-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



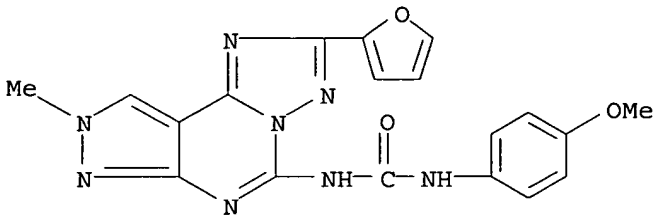
RN 252979-48-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



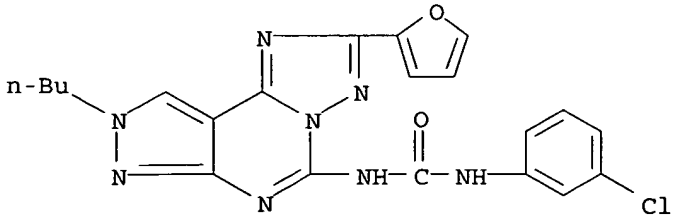
RN 261629-22-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



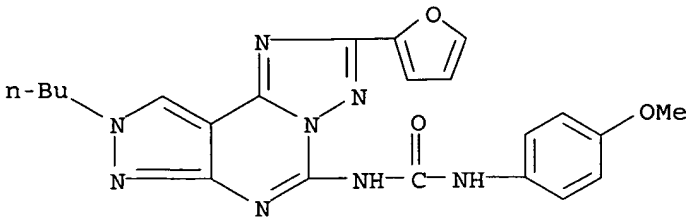
RN 261629-23-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-methyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



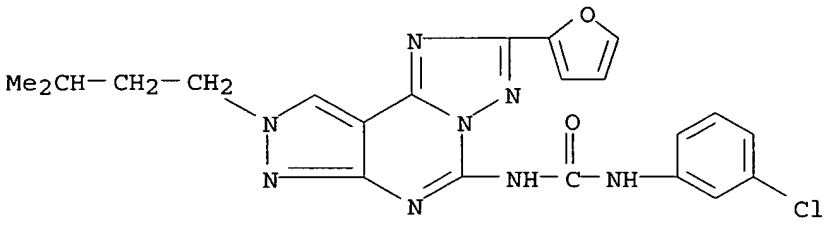
RN 261629-24-7 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



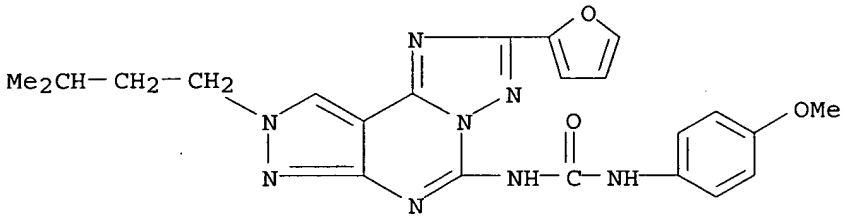
RN 261629-25-8 CAPLUS
CN Urea, N-[8-butyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



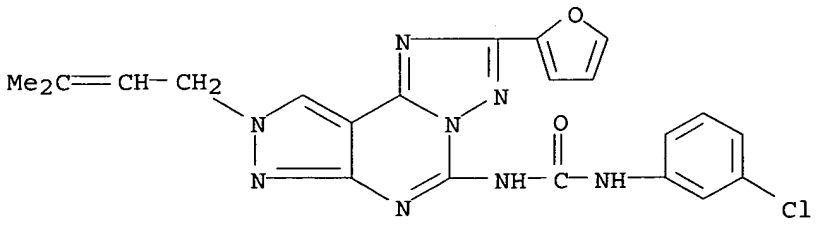
RN 261629-26-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



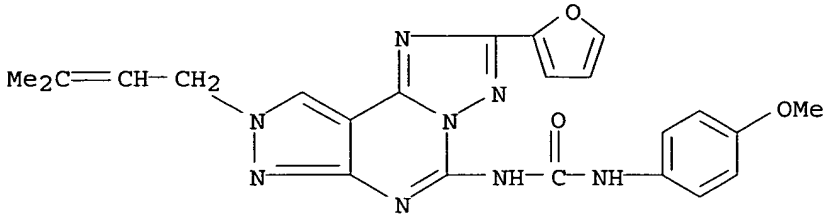
RN 261629-27-0 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



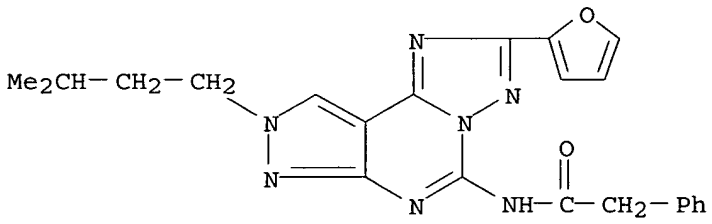
RN 261629-28-1 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



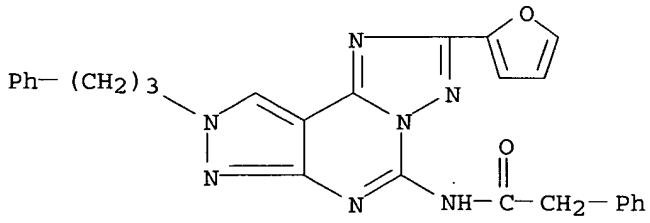
RN 261629-29-2 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-methyl-2-butenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



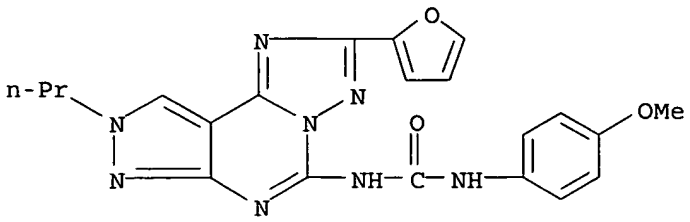
RN 261629-30-5 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-(3-methylbutyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 261629-31-6 CAPLUS
CN Benzeneacetamide, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

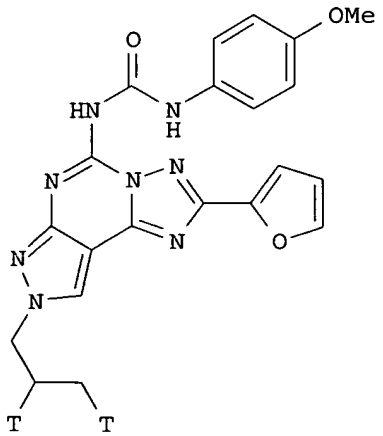


IT **261629-32-7**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(triazolopyrimidine adenosine A3 receptor modulator preparation and therapeutic and diagnostic use)
RN 261629-32-7 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)-, labeled with tritium (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:146874 CAPLUS
DOCUMENT NUMBER: 132:290670
TITLE: Synthesis and preliminary biological evaluation of [3H]-MRE 3008-F20: the first high affinity radioligand antagonist for the human A3 adenosine receptors
AUTHOR(S): Baraldi, Pier Giovanni; Cacciari, Barbara; Romagnoli, Romeo; Varani, Katia; Merighi, Stefania; Gessi, Stefania; Borea, Pier Andrea; Leung, Edward; Hickey, Sarah L.; Spalluto, Giampiero
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(3), 209-211
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

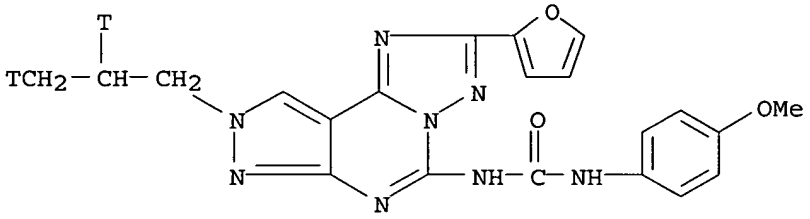
AB The synthesis and the preliminary biol. evaluation of the first high affinity radioligand antagonist for the human A3 adenosine receptor, pyrazolotriazolopyrimidinyl methoxyphenyl urea I ([3H]-MRE 3008-F20) are reported. I bound human A3 receptors expressed in CHO cells with KD and Bmax value of 0.82 ± 0.08 nM and 297 ± 28 fmol/mg of protein, resp. I represents a useful tool for further characterization of A3 adenosine

receptor subtypes.

IT **264623-55-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of a tritiated pyrazolotriazolopyrimidiyl methoxyphenyl urea as a radiolabeled adenosine A3 receptor antagonist)

RN 264623-55-4 CAPLUS

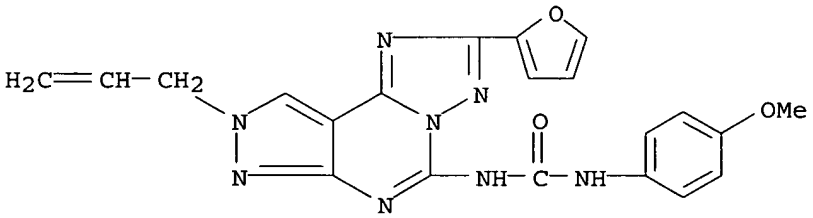
CN Urea, N-[2-(2-furanyl)-8-(propyl-2,3-t2)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



IT **264623-54-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of a tritiated pyrazolotriazolopyrimidiyl methoxyphenyl urea as a radiolabeled adenosine A3 receptor antagonist)

RN 264623-54-3 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-(2-propenyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:144672 CAPLUS

DOCUMENT NUMBER: 132:175820

TITLE: The use of adenosine A1 and/or A3 receptor antagonists to inhibit tumor growth and metastasis, and combinations with other agents

INVENTOR(S): Leung, Edward

PATENT ASSIGNEE(S): Medco Research, Inc., USA

SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

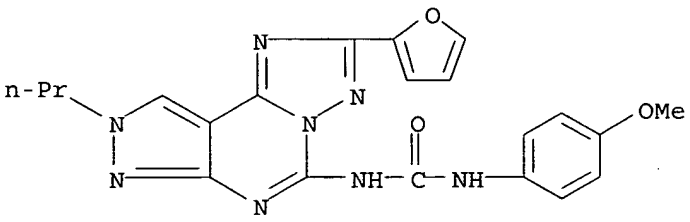
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010391	A1	20000302	WO 1999-US18817	19990824
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6326390	B1	20011204	US 1999-377271	19990819
AU 9955712	A1	20000314	AU 1999-55712	19990824
PRIORITY APPLN. INFO.:			US 1998-97852P P	19980825
			WO 1999-US18817 W	19990824

AB Tumor growth and metastasis can be inhibited by administration of adenosine A1 and/or A3 antagonists, preferably A3 antagonists, to a patient. The antagonists can be, and preferably are, administered in combination with other anti-tumor agents, e.g. antiangiogenic agents (including adenosine A2a antagonists) and/or cytotoxic agents. The cytotoxic agents attack the tumor cells themselves, and the anti-angiogenic agents prevent the growth of vasculature which would otherwise support the growth of the tumor cells. Characterization of A3 receptors in some human tumor cell lines is also described.

IT **252979-43-4D**, tritiated analogs
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(adenosine A1 and/or A3 receptor antagonists to inhibit tumor growth and metastasis, and combinations with other agents)

RN 252979-43-4 CAPLUS

CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

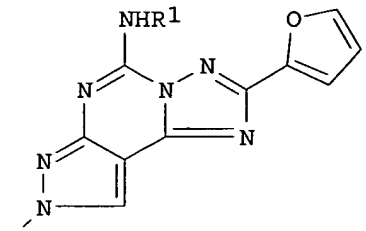
ACCESSION NUMBER: 1999:643387 CAPLUS

DOCUMENT NUMBER: 132:49935

TITLE: Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine derivatives as highly potent and selective human A3 adenosine receptor antagonists

AUTHOR(S): Baraldi, Pier Giovanni; Cacciari, Barbara; Romagnoli, Romeo; Spalluto, Giampiero; Klotz, Karl-Norbert; Leung, Edward; Varani, Katia; Gessi, Stefania;

Merighi, Stefania; Borea, Pier Andrea
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche and Dipartimento di Medicina Clinica e Sperimentale-Sezione di Farmacologia, Universita degli Studi di Ferrara, Ferrara, I-44100, Italy
SOURCE: Journal of Medicinal Chemistry (1999), 42(22), 4473-4478
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



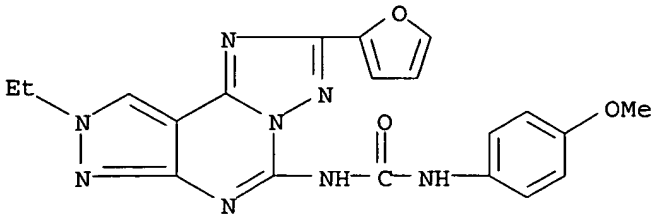
I

AB The pyrazolotriazolopyrimidines I (R = Ph, Pr, PhCH2CH2, PhCH2CH2CH2; R1 = H, 4-MeOC6H4NHCO, 3-ClC6H4NHCO) were prepared and the structural requirements necessary for recognition by the A3 adenosine receptor were studied. A substituted phenylcarbamoyl moiety confers affinity and selectivity for the A3 adenosine receptor subtype at the pyrazolotriazolopyrimidine nucleus, while the N5-unsubstituted derivs. lack both affinity and selectivity for human A3 receptors, showing high affinity for A1 and/or A2A receptor subtypes. Substitution at the N8 position with small alkyl groups resulted in higher affinity and selectivity at the human A3 receptor. When N8-Et and N5-4-methoxyphenylcarbamoyl substitutions were combined, the most potent and selective human A3 adenosine antagonist I (R = Et; R1 = 4-MeOC6H4NHCO) was obtained. Thus, the pyrazolotriazolopyrimidine nucleus is a possible template for generating adenosine receptor subtype-selective ligands.

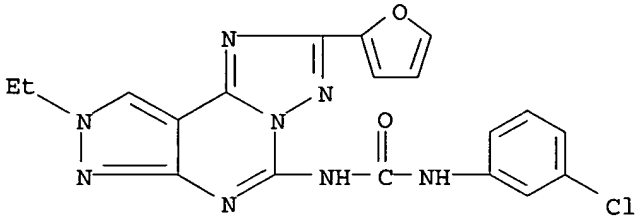
IT **252979-41-2P 252979-42-3P 252979-43-4P**
252979-44-5P 252979-45-6P 252979-46-7P
252979-47-8P 252979-48-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-A3-adenosine receptor antagonist activities of aminopyrazolotriazolopyrimidines)

RN 252979-41-2 CAPLUS

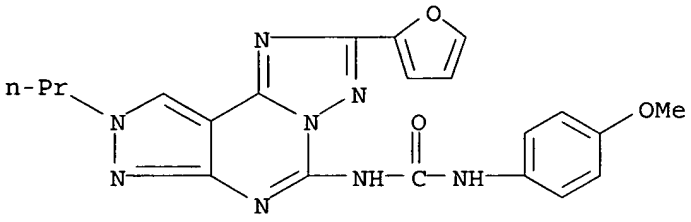
CN Urea, N-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



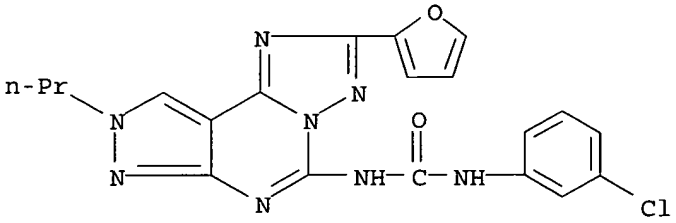
RN 252979-42-3 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[8-ethyl-2-(2-furanyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



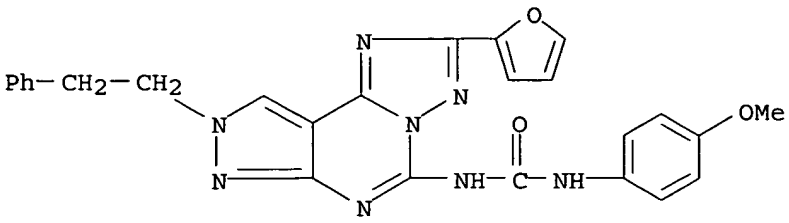
RN 252979-43-4 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



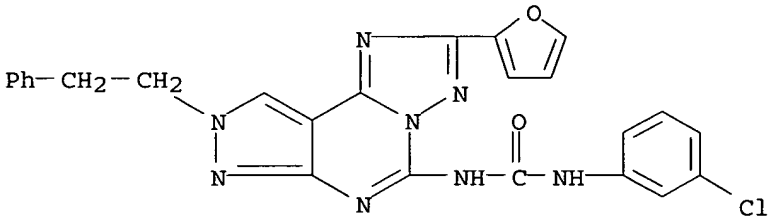
RN 252979-44-5 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-propyl-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



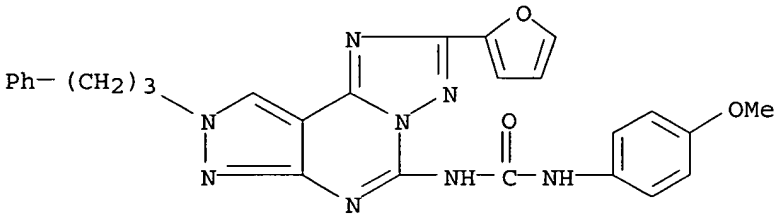
RN 252979-45-6 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



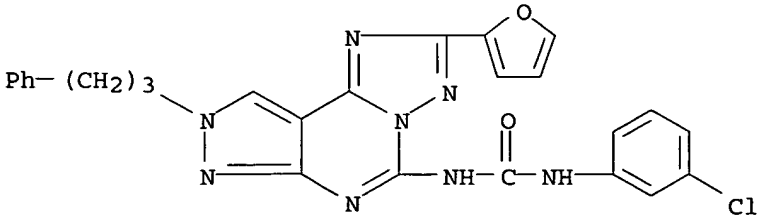
RN 252979-46-7 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(2-phenylethyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 252979-47-8 CAPLUS
CN Urea, N-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]-N'-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 252979-48-9 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-[2-(2-furanyl)-8-(3-phenylpropyl)-8H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:95632 CAPLUS
DOCUMENT NUMBER: 124:232366

TITLE: Pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine Derivatives: Potent and Selective A2A Adenosine Antagonists

AUTHOR(S): Baraldi, Pier Giovanni; Cacciari, Barbara; Spalluto, Giampiero; Pineda de Villatoro, Maria Jose; Zocchi, Cristina; Dionisotti, Silvio; Ongini, Ennio
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita degli Studi di Ferrara, Ferrara, 44100, Italy

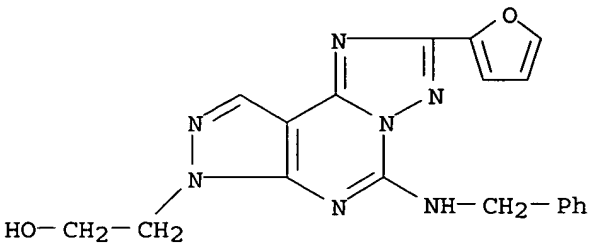
SOURCE: Journal of Medicinal Chemistry (1996), 39(5), 1164-71
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine derivs. bearing alkyl and aralkyl chains on positions 7 and 8, were synthesized in the attempt to obtain potent and selective antagonists for the A2A adenosine receptor subtype. The compds. were tested in binding and functional assays to evaluate their potency for the A2A compared with the A1 adenosine receptor subtype. In binding studies in rat brain membranes, most of the compds. showed affinity for A2A receptors in the low nanomolar range with a different degree of A2A vs. A1 selectivity. Comparison of N7- and N8-substituted pyrazolo derivs. indicates that N7 substitution decreases the A1 affinity with the concomitant increase of A2A selectivity. Specifically, the introduction of a 3-phenylpropyl group at pyrazolo nitrogen in position 7 increased significantly the A2A selectivity, being 210-fold, while the A2A receptor affinity remained high (Ki = 2.4 nM). With regards to the affinity for A2A receptors, also the compound bearing in the 7-position a β-morpholin-4-ylethyl group, deserves attention (Ki = 5.6 nM). Conversely, the N7-4-phenylbutyl derivative showed a remarkable selectivity (A1/A2A ratio = 129) associated with lower A2A affinity (Ki = 21 nM). In functional studies, most of the compds. examined reversed 5'-(N-ethylcarbamoyl)adenosine-induced inhibition of rabbit platelet aggregation inhibition which is a biol. response mediated by the A2A receptor subtype. The compds. are potent and selective A2A antagonists which can be useful to elucidate the pathophysiol. role of this adenosine receptor subtype which seems to be involved in neurodegenerative disorders such as Parkinson's disease.

IT **174648-49-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and adenosine antagonistic activity of)

RN 174648-49-8 CAPLUS

CN 7H-Pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidine-7-ethanol, 2-(2-furanyl)-5-[(phenylmethyl)amino]- (9CI) (CA INDEX NAME)


O
N
N
N
N
N
NH— CH2— Ph
HO— CH2— CH2